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(74) Agents: **POTTER, Jane, E., R.**; Seed Intellectual Prop-
erty Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seat-
tle, WA 98104-7092 et al. (US).

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(71) Applicant (for all designated States except US): **CORIXA CORPORATION** [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).

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(72) Inventors; and

(75) Inventors/Applicants (for US only): **MEAGHER, Madeleine, Joy** [US/US]; 507 N.E. 71st #1, Seattle, WA 98115 (US). **XU, Jiangchun** [US/US]; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). **KING, Gordon, E.** [US/US]; 15716 First Avenue N.W., Shoreline, WA 98117 (US).

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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF COLON CANCER

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF COLON CANCER

TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of
5 cancer, such as colon cancer. The invention is more specifically related to polypeptides
comprising at least a portion of a colon tumor protein, and to polynucleotides encoding
such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and
pharmaceutical compositions for prevention and treatment of colon cancers, and for the
diagnosis and monitoring of such cancers.

10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although
advances have been made in detection and therapy of cancer, no vaccine or other
universally successful method for prevention or treatment is currently available.
Current therapies, which are generally based on a combination of chemotherapy or
15 surgery and radiation, continue to prove inadequate in many patients.

Colon cancer is the second most frequently diagnosed malignancy in the
United States as well as the second most common cause of cancer death. An estimated
95,600 new cases of colon cancer will be diagnosed in 1998, with an estimated 47,700
deaths. The five-year survival rate for patients with colorectal cancer detected in an
20 early localized stage is 92%; unfortunately, only 37% of colorectal cancer is diagnosed
at this stage. The survival rate drops to 64% if the cancer is allowed to spread to
adjacent organs or lymph nodes, and to 7% in patients with distant metastases.

The prognosis of colon cancer is directly related to the degree of
penetration of the tumor through the bowel wall and the presence or absence of nodal
25 involvement, consequently, early detection and treatment are especially important.
Currently, diagnosis is aided by the use of screening assays for fecal occult blood,
sigmoidoscopy, colonoscopy and double contrast barium enemas. Treatment regimens
are determined by the type and stage of the cancer, and include surgery, radiation
therapy and/or chemotherapy. Recurrence following surgery (the most common form

of therapy) is a major problem and is often the ultimate cause of death. In spite of considerable research into therapies for the disease, colon cancer remains difficult to diagnose and treat. In spite of considerable research into therapies for these and other cancers, colon cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as colon cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a colon tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NOs:1-1556; (b) variants of a sequence recited in SEQ ID NO: 1-1556; and (c) complements of a sequence of (a) or (b).

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a colon tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a colon tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B
5 cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins
10 that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

15 Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
20 patient a pharmaceutical composition or vaccine as recited above. The patient may be afflicted with colon cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological
25 sample with T cells that specifically react with a colon tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological
30 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating $CD4^{+}$ and/or $CD8^{+}$ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a colon tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be colon cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as

diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as colon cancer. The compositions described herein may include colon tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a colon tumor protein or a variant thereof. A "colon tumor protein" is a protein that is expressed in colon tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain colon tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with colon cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human colon tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NOs:1-1556.

COLON TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a colon tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a colon tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a colon tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a colon tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native colon tumor protein or a portion thereof. The term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman-Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring

DNA sequence encoding a native colon tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC
5 containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides
10 that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need
15 not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that
20 is at least two fold greater in a colon tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively,
25 polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as colon tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

30 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a colon tumor cDNA library) using well known techniques.

Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation

and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of
5 amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer,
10 which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

15 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences
20 may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of colon tumor proteins are provided in SEQ ID NOs: 1-1556.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase
25 phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a colon tumor protein, or portion thereof, provided that the
30 DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as

described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a colon tumor polypeptide, and administering the transfected cells to the patient).

5 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells or tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor
10 protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to
15 hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

 A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled
20 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

 Any polynucleotide may be further modified to increase stability *in vivo*.
25 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-, methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

30 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For

example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

COLON TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a colon tumor protein or a variant thereof, as

described herein. As noted above, a "colon tumor protein" is a protein that is expressed by colon tumor cells. Proteins that are colon tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with colon cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a colon tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native colon tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be

immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native colon
5 tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native colon tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be
10 diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or
15 transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity
20 (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the
25 polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups
30 having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine.

Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from
5 a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader)
10 sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

15 Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector
20 containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells, such as mammalian cells and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated
25 using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having less than about 100 amino acids, and
30 generally less than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such

polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is

incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided. Such proteins comprise a polypeptide as described herein together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the

N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1
5 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine
10 amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing
15 plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion
20 incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural
25 system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a colon tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a colon tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a colon tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as colon cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a colon tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an

antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation
5 of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.,* mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the
10 immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled
15 periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J.*
20 *Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.,* reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a
25 myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine,
30 aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture

supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-

containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an
5 antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

10 It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references
15 describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the
20 intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell
25 et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent
30 may be prepared in a variety of ways. For example, more than one agent may be

coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a colon tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO

92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a colon tumor polypeptide, polynucleotide encoding a colon tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a colon tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a colon tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a colon tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a colon tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Colon tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are

derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a colon tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a colon tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a colon tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a colon tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents described herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells. It will be apparent that a vaccine may comprise both a polynucleotide and a polypeptide component. Such vaccines may provide for an enhanced immune response.

It will be apparent that a vaccine may contain pharmaceutically acceptable salts of the polynucleotides and polypeptides provided herein. Such salts

may be prepared from pharmaceutically acceptable non-toxic bases, including organic bases (*e.g.*, salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (*e.g.*, sodium, potassium, lithium, ammonium, calcium and magnesium salts).

5 While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous
10 or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres
15 (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 5,814,344 and 5,942,252.

Such compositions may also comprise buffers (*e.g.*, neutral buffered
20 saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives.
25 Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a
30 substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

Bordetella pertussis or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10 Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

 Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.
25 MPL adjuvants are available from Corixa Corporation (Seattle, WA; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with
5 cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France),
10 SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

15 Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of
20 compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.*, Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained
25 within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-
30 release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and,

optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of
5 cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation,
10 maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are
15 characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules
20 (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a colon tumor protein (or portion or other variant thereof) such that the colon tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such
25 transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO
30 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by

incubating dendritic cells or progenitor cells with the colon tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

15 CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as colon cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. Administration may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided
5 herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host
10 immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody
15 receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

20 Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of
25 cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides
30 or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a

polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive
5 long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced
10 into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical
15 compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for
20 individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor
25 cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose
30 ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a colon tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

10 METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more colon tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as colon cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a colon tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the

remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length colon tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about

10 μg , and preferably about 100 ng to about 1 μg , is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with
5 both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at
10 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.
15 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

20 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to
25 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with colon cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of
30 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium

may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support
5 with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.
10 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are
15 generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of
20 the reaction products.

To determine the presence or absence of a cancer, such as colon cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average
25 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*
30 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot

of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample
5 generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

10 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution
15 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.
20 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the
25 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about
30 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use
5 colon tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such colon tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a colon tumor protein in a biological sample. Within
10 certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a colon tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells.
15 For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of colon tumor polypeptide to serve as a control. For CD4⁺ T cells,
20 activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

25 As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a colon tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a colon tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for
30 (*i.e.*, hybridizes to) a polynucleotide encoding the colon tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as

gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a colon tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers
5 and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a colon tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a
10 polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule
15 having a sequence recited in SEQ ID NOs:1-1556. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in
20 conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and
25 from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

30 In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described

above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the
5 level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound
10 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple colon tumor protein markers may be assayed within a given sample. It will be apparent that binding agents
15 specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

20 DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may
25 contain a monoclonal antibody or fragment thereof that specifically binds to a colon tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable
30 for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a colon tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a colon tumor protein. Such an oligonucleotide may be used, 5 for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a colon tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1

IDENTIFICATION OF COLON TUMOR PROTEIN cDNAs

This Example illustrates the identification of cDNA molecules encoding
5 colon tumor proteins using PCR-based cDNA subtraction methodology.

A pool of tester mRNA was collected from three colon adenocarcinoma
samples showing moderate histological differentiation and no evidence of metastasis.
Eight normal tissues, including brain, pancreas, bone marrow, liver, heart, lung,
stomach and small intestine were represented in the driver mRNA pool. cDNA
10 synthesis, hybridization and PCR amplification were performed according to the
methods of Clontech (Palo Alto, CA), with minor modifications. In a first subtraction,
the restriction enzymes PvuII, DraI, MscI and StuI were used to digest cDNAs. The
tester to driver ratio was 1:40. In a second subtraction, DraI, MscI and StuI were used
for cDNA digestion. A tester to driver ratio of 1:76 was employed. Following the PCR
15 amplification steps, the cDNAs were cloned into the pCR2.1 plasmid vector. The
libraries resulting from the first and second subtractions, named CPS1 and CPS2,
respectively, were used to obtain clones for microarray analysis and sequencing. Inserts
were PCR amplified and purified. Each clone was sequenced from one direction with
either M13 Forward primer or M13 Reverse primer. The determined cDNA sequences
20 for 1535 of the isolated clones are provided in SEQ ID NOs:1-1556.

A cDNA library was constructed in the PCR2.1 vector (Invitrogen,
Carlsbad, CA) by subtracting a pool of three colon tumors with a pool of normal colon,
spleen, brain, liver, kidney, lung, stomach and small intestine using PCR subtraction
methodologies (Clontech, Palo Alto, CA). The subtraction was performed using a
25 PCR-based protocol, which was modified to generate larger fragments. Within this
protocol, tester and driver double stranded cDNA were separately digested with five
restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII,
SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than
the average size of 300 bp that results from digestion with RsaI according to the
30 Clontech protocol. This modification did not affect the subtraction efficiency. Two

tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the
5 two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to
10 populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed
15 using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially
20 expressed cDNAs so that rare transcripts that are over-expressed in colon tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

To characterize the complexity and redundancy of the subtracted library, 96 clones were randomly picked and 65 were sequenced, as previously described.
25 These sequences were further characterized by comparison with the most recent Genbank database (April, 1998) to determine their degree of novelty. No significant homologies were found to 21 of these clones, hereinafter referred to as 11092, 11093, 11096, 11098, 11103, 11174, 11108, 11112, 11115, 11117, 11118, 11134, 11151, 11154, 11158, 11168, 11172, 11175, 11184, 11185 and 11187. The determined cDNA
30 sequences for these clones are provided in SEQ ID NO: 48, 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101 and 109-111, respectively.

Two-thousand clones from the above mentioned cDNA subtraction library were randomly picked and submitted to a round of PCR amplification. Briefly, 0.5 µl of glycerol stock solution was added to 99.5 µl of pcr MIX (80 µl H₂O, 10 µl 10X PCR Buffer, 6 µl 25 mM MgCl₂, 1 µl 10 mM dNTPs, 1 µl 100 mM M13 forward primer (CACGACGTTGTAAAACGACGG), 1 µl 100 mM M13 reverse primer (CACAGGAAACAGCTATGACC)), and 0.5 µl 5 u/ml Taq polymerase (primers provided by (Operon Technologies, Alameda, CA). The PCR amplification was run for thirty cycles under the following conditions: 95°C for 5 min., 92°C for 30 sec., 57°C for 40 sec., 75°C for 2 min. and 75°C for 5 minutes.

10 mRNA expression levels for representative clones were determined using microarray technology (Synteni, Palo Alto, CA) in colon tumor tissues (n=25), normal colon tissues (n=6), kidney, lung, liver, brain, heart, esophagus, small intestine, stomach, pancreas, adrenal gland, salivary gland, resting PBMC, activated PBMC, bone marrow, dendritic cells, spinal cord, blood vessels, skeletal muscle, skin, breast and fetal tissues. The number of tissue samples tested in each case was one (n=1), except where specifically noted above; additionally, all the above-mentioned tissues were derived from humans. The PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, and fluorescent-labeled cDNA probes were generated by reverse transcription according to the protocol provided by Synteni. The microarrays were probed with the labeled cDNA probes, the slides scanned, and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.

Clones corresponding to SEQ ID Nos:1506-1556 were overexpressed in colon tumors and showed low or no expression levels in normal tissues.

EXAMPLE 2

SYNTHESIS OF POLYPEPTIDES

30 Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-

Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following

5 cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water

10 (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration,

15 various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NOs:1-1556;
- (b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and
- (c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polynucleotide encoding at least 15 amino acid residues of a colon tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing sequences.

4. An isolated polynucleotide encoding a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing sequences.

5. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NOs:1-1556.

6. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions.

7. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 3-6.

8. An expression vector, comprising a polynucleotide according to any one of claims 3-7.

9. A host cell transformed or transfected with an expression vector according to claim 8.

10. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a colon tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs1-1556 or a complement of any of the foregoing polynucleotide sequences.

11. A fusion protein, comprising at least one polypeptide according to claim 1.

12. A fusion protein according to claim 11, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

13. A fusion protein according to claim 11, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

14. A fusion protein according to claim 11, wherein the fusion protein comprises an affinity tag.

15. An isolated polynucleotide encoding a fusion protein according to claim 11.

16. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 3;
- (c) an antibody according to claim 10;
- (d) a fusion protein according to claim 11; and
- (e) a polynucleotide according to claim 15.

17. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 3;
- (c) an antibody according to claim 10;
- (d) a fusion protein according to claim 11; and
- (e) a polynucleotide according to claim 15.

18. A vaccine according to claim 17, wherein the immunostimulant is an adjuvant.

19. A vaccine according to any claim 17, wherein the immunostimulant induces a predominantly Type I response.

20. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 16.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 17.

22. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

23. A pharmaceutical composition according to claim 22, wherein the antigen presenting cell is a dendritic cell or a macrophage.

24. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NOs:1-1556;
 - (b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and
 - (c) complements of sequences of (i) or (ii);
- in combination with an immunostimulant.

25. A vaccine according to claim 24, wherein the immunostimulant is an adjuvant.

26. A vaccine according to claim 24, wherein the immunostimulant induces a predominantly Type I response.

27. A vaccine according to claim 24, wherein the antigen-presenting cell is a dendritic cell.

28. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NOs:1-1556;
 - (b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and
 - (c) complements of sequences encoded by a polynucleotide recited in any one of SEQ ID NOs:1-1556;
- and thereby inhibiting the development of a cancer in the patient.

29. A method according to claim 28, wherein the antigen-presenting cell is a dendritic cell.

30. A method according to any one of claims 20, 21 and 28, wherein the cancer is colon cancer.

31. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NOs:1-1556; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

32. A method according to claim 31, wherein the biological sample is blood or a fraction thereof.

33. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

34. A method for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NOs:1-1556;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

35. An isolated T cell population, comprising T cells prepared according to the method of claim 34.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs:1-1556;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an

amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (1) sequences recited in SEQ ID NOs:1-1556;
- (2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:1-1556 under moderately stringent conditions; and

- (3) complements of sequences of (1) or (2);

- (ii) polynucleotides encoding a polypeptide of (i); and

- (iii) antigen presenting cells that express a polypeptide of (i);

such that T cells proliferate;

- (b) cloning at least one proliferated cell to provide cloned T cells;

and

- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing polynucleotide sequences;

- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

40. A method according to claim 39, wherein the binding agent is an antibody.

41. A method according to claim 42, wherein the antibody is a monoclonal antibody.

42. A method according to claim 39, wherein the cancer is colon cancer.

43. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

44. A method according to claim 43, wherein the binding agent is an antibody.

45. A method according to claim 44, wherein the antibody is a monoclonal antibody.

46. A method according to claim 43, wherein the cancer is a colon cancer.

47. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO:1-1556 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

48. A method according to claim 47, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

49. A method according to claim 47, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

50. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO:1-1556 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 10; and
- (b) a detection reagent comprising a reporter group.

54. A kit according to claim 53, wherein the antibodies are immobilized on a solid support.

55. A kit according to claim 53, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

56. A kit according to claim 53, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

57. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a

colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-1556 or a complement of any of the foregoing polynucleotides.

58. A oligonucleotide according to claim 57, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NOs:1-1556.

59. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 58; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

SEQUENCE LISTING

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451

<210> 16<211> 452<212> DNA<213> Homo sapien
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180gtatattacat tatgaatgta taaccagagc atgatttgta aagccgacag tatgtttcta
240ttacacaaca ctttttgata cagcgtctct tgtcttcaact gatactggag tctcogttgt
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452

<210> 17<211> 244<212> DNA<213> Homo sapien
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120agaacctcta caggttatgc agcaagttct taatattatt tcccttctgt ggaaactctc
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240tttt
244

<210> 18<211> 84<212> DNA<213> Homo sapien
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84

<210> 19<211> 312<212> DNA<213> Homo sapien
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120agttccgagg tcttggggcc ctcttcaagt cctcgctga gcccgaggcc ctcaccgagt
180cagagacgga gtatgtcatc cgctgcacca aacacacctt caccaaccac atgggttttc
240agtttgactg cacaacacac ctcaatgacc agaccttgga gaatgtcaca gtgcagatgg
300agcccactga gg
312

<210> 20<211> 420<212> DNA<213> Homo sapien
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120tcccatcggc ttgatctctt gtatctgcc cgccttttn ctctgcaaaa agcctgggat
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 240caacgtctgc cttecgtagg ctgacatcgc gggacccgc tgccttcctc tcttcaactg
 300ccacatagac ggntgcaatc tctccatana agtggncctg cttcacttca caccagtacc
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 420

<210> 21<211> 435<212> DNA<213> Homo sapien .

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 120gcccaccaag ctgtcactgc tgcactcact ctgcaaggga tcaggaccag caacctttat
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 240caaatacc aaatttttgc gtatgtttat attgtatngt tctaaataat gggtagnctg
 300tgaaataaga tcttgccacc catgtaataa tantagtaat actatagtna naaatggctg
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<210> 22<211> 407<212> DNA<213> Homo sapien

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 120gccaccccccac ttacatttcc tactatacaa tgcctttttg gcgcttgata aatcaagcat
 180tcatgtagca ttacattcaa cagaaacatt tctogtactt tgggtttaag atccttgtcc
 240ctccagntcg gatgtcgtga catctgactc ttcttcattg taaatatttt canccatttg
 300ccatatctgc atgatgttat cctcagacac tgagcaaatg acccaaggct nattgggggt
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 407

<210> 23<211> 272<212> DNA<213> Homo sapien

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 120caaaaacctg tttttgaatc cccaagaagg cagcatgtgt atacaacat accaccttgc
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 272

<210> 24<211> 424<212> DNA<213> Homo sapien

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 120agataagaaa gttgaaacaa aggtttgtaa agtctcctga actattoagt ttaataacca
 180attatccctc aatattacaa aataaaatga ctggatcaat gntgactott ctttgataatc
 240atttataaaa tgccttgata ttacttacta agttccctga taactcaaac aaggtaaaat
 300taacactttc attttcaggt attgtctttt tagaagagga ttaccacttt catttagatg
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 424

<210> 25<211> 372<212> DNA<213> Homo sapien

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 180actcattcat ntgtcctggt ctgatccct tggcatcccg ggtoaggatc tggttctcta
 240cctcattgat ggnocctggct gatggnnngt gagcatctgn tcccatccca cacggatng
 300ctccatgggt tagttgggtg gcttgtnnc taagatgagc ggctcctgga tganctggtn
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 372

<210> 26<211> 342<212> DNA<213> Homo sapien

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 120atctgggaaa tgaatgaata agtactctgt ggctaccagt tgcattatgg agtcacctag
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342

<210> 27<211> 315<212> DNA<213> Homo sapien

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120ggtttgggtt anacgtccgg gaattgcac tgtttttaag cctaattggg ggacagctca
180tgagtgaag acgtcttgat atgtaattat tatacgaatg ggggttcaa tcgggagtac
240tactogattg tcaacgtcaa ggagtcgcag gtcgcctggt tctaggaata atgggggaag
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315

<210> 28<211> 311<212> DNA<213> Homo sapien

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120ccagttgctg ctganctgct gnggaaggct gttgattcct gaccaatgct tgnatggtgt
180gaggggtggc aggtaacact gtgtgagtga ancctgggct gtcactggaa ggggtgnaat
240tgtnactat aaatggaca tntgtgctcg cttgtcnaga aactctcngn tttcacngn
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311

<210> 29<211> 516<212> DNA<213> Homo sapien

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120cacagagttt gtaatagttg ttgtggacag tacagacaga gagaggattt ctgtaactag
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420gacctcttct ctgatttttg tataaatgaa ggtgctggac tttacctgaa agctgcaaaa
480attaatggtt tagatatatt nataataaac tgattt
516

<210> 30<211> 355<212> DNA<213> Homo sapien

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60acttcagcag catgaagaag tactgccaag tcatccgtgt cattgcccac acccagatgc
120gcctgcttcc tctgcgccag aagaaggccc acctgatgga gatccagggtg aacggaggca
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240aagtgttttg gcaggatgag atgatcgacg tcatcggggt gaccaagggc aaaggctaca
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355

<210> 31<211> 355<212> DNA<213> Homo sapien

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120ttacttcatg tgggtctgga tggaagatta gtggcctac aggatcattt atttatattg
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240ctcttccatt tgactggtct attgaataat tttttttct ttaagcttat gagacatggg
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355

<210> 32<211> 285<212> DNA<213> Homo sapien

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120gcagggcacg ctctgtgttc ctccgtgcca cccggatcag gtagaccatg gaggtccca
180ggaaggagat caacaccatc acgaacagcc ccgcagaac caccacctt gagccaaggg
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285

<210> 33<211> 250<212> DNA<213> Homo sapien

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60agaacctacg cacctacgtg aggagcttag ccagaaatgg gatggactga acggacagtt
120ccagaagtgt gactggctaa agctcgatgt ggacacagct gtatagctgc ttccagtgtg
180gacggagccc tggcatgtca acagcggtcc tagagaagac aggctggaag atagctgtga
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250

<210> 34<211> 455<212> DNA<213> Homo sapien

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455

<210> 35<211> 409<212> DNA<213> Homo sapien

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300gaaacttacc caagcaacgt aattcctgtt ttcattgggtc ctgtanagt ttgagtcacg
360aaggtaangc nggggagtga ctgaataaac tctgnctttt acctcggca
409

<210> 36<211> 225<212> DNA<213> Homo sapien

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120tttcaacttc cagctttctg tctaattgct gtgtgccaat ggcttgagtt aggttgctc
180tttaggactt cagtagctat tctcatcctt cttgggggac acaaa
225

<210> 37<211> 267<212> DNA<213> Homo sapien

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120caagaccacg ttgtgtcgg ccaccagctc agggccctca tagaatcgca cctgatgta
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240gtttngcggg tccttcacac gnagccg
267

<210> 38<211> 556<212> DNA<213> Homo sapien

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180aaaattaact ttagaaaaag ggaaggatgt tgtgtaaaat caagtcaatt atttgaggnt
240tttataatat tgagtactta tgtactaagt cacaccagc cagtcaataa ctgagaaatc
300aaaataaaa aataatttca aagaattaca taaatacagg gccttttgag atttttgna
360ttgttaacaa aaacgaatgg tttttacaat tcagtgtaat tctacgaata tttatttggc
420cccatgttag gcactgangc tncacagcaa gngaaataga cctcggnncc cgaccacgct
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556

<210> 39<211> 203<212> DNA<213> Homo sapien

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60atctcactca agcaaagttc cactaactta tatatttcaa gtgttttgta accaagaagg
120ggaggggagaa gagattcgat tctgagcttc ctactcccg gttctgcgta gagaagccga
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203

<210> 40<211> 560<212> DNA<213> Homo sapien

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420gntcaccct gtagaagnt ccatcgtaac caaagtcac aacccccacc gnttacacaa
480ccttgccccg ggcggnccgc caaagggcga aattcttgca gnataccca tcacacctg
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560

<210> 41<211> 265<212> DNA<213> Homo sapien

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120ggacctccat ggaaggcagt ttgtgaata tccggagaac ttggaagtga ctttcaggat
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265

<210> 42<211> 407<212> DNA<213> Homo sapien

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120ttttggcgat aaagagaact tgtgtgtgtt gctgcggtat ccattgata cgccaagaat
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407

<210> 43<211> 343<212> DNA<213> Homo sapien

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240cgagagctc gcaagttcat cccctcttcc ctgaggtctg ttggctggag gctgcagaac
300attggtgatg acatggacac ctgcccggcg gccgctcgaa ggg
343

<210> 44<211> 186<212> DNA<213> Homo sapien

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120tccaatctgc cagtcttctt gaaatatcga aaatacacca gggctgctat atcagagcca
180ccctgg
186

<210> 45<211> 503<212> DNA<213> Homo sapien

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120aacagcactt ccaggccctt gcctttaaga actccttaaa ggcaaagtng gacacatgcc
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360gaggtgggac ctgcgncgn gaccacnctn agggcgaaat tctncagata tccatcacac
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503

<210> 46<211> 559<212> DNA<213> Homo sapien

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120cgagtcccgt gccataggcg gacaccaggg caggggtccc cgcttggtcca ngctcccca
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<210> 47<211> 513<212> DNA<213> Homo sapien
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 120ttatttttaca gaagtatggc aagtttaca agcaatatct aaatctaatt atcattagtt
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 420cctctacaat tattttcttt aagctgantg ctncctccct ggaatattca tgttttctcc
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 513

<210> 48<211> 413<212> DNA<213> Homo sapien
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 413

<210> 49<211> 560<212> DNA<213> Homo sapien
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 560

<210> 50<211> 231<212> DNA<213> Homo sapien
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 120agccaagggt ggtgtccatt tctgggaatg gttaaacaca aaaggctgat agctggtatc
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 231

<210> 51<211> 265<212> DNA<213> Homo sapien
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 120gtgaggcgaa ttctggggct gctggatgct tacttgaaga cgaggacttt tctgggtggc
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 265

<210> 52<211> 318<212> DNA<213> Homo sapien
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120tcctctgatac aggggtgagca tcaaaactcaa actacgccct gatcggcgca ctgcgagcag
180tagcccaaac aatctcatat gaagtcaccc tagccatcat tctactatca acattactaa
240taagtggctc ctttaacctc tccaccctta tcacaacaca agaacacctc tgattactcc
300tgccatcatg acccttgg
318

<210> 53<211> 335<212> DNA<213> Homo sapien
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60gttggtgggca acttgcatcg gctgggagtc accaacacca ttatcagcca ctatgatggg
120cgccagttcc ccaagggtgt ggggggcttt gaccgagtac tgctggatgc tccctgcagt
180ggcactgggg tcatctccaa ggatccagcc gtgaagacta acaaggatga gaaggacatc
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300acctccaaga caggaggcta cctgggttac tgcac
335

<210> 54<211> 280<212> DNA<213> Homo sapien
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60agcaaaaacag caaccgattt ctgcttttca tgtaggtgtg ttccacgta taaacatttt
120gaagcctctt acaaaattat ttacatcggt tgtcatctat ttacatcttt taagagcaac
180tttttctaaca acaaaaacta taacttatca agttatgaaa attgtcttct aaaaaaactt
240actatattac cacaaaataa ataaagataa acaatatattt
280

<210> 55<211> 559<212> DNA<213> Homo sapien
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60atggctgatt tataatagtc acaggctttg ttgtggtggt tacaggcttt gttgtggtgg
120tcaccggctt cgtcgtagtc accggcttcg ttgtcgtcac tgggttggtg taggacttg
180aagtaacgtt attcggaaca ttacttgtt tgtgaccaa cttcacaagg ttctttgtgg
240gttggtcccc ttggaaccaa tcacactggt tctgatatc tggggacaag taaaagcat
300tttctactgt gacgaaggat ggcaacagcc tcccgaagcg catcaaaggc tccctggtga
360gctcgggtga cttgtccact aatttgaana aacgtcgttt ggctcactgg cgaagggtga
420tacctcttga tgttcacctt ccttgccnat gccaggacc acgaaanaaa tancccttgc
480atttgnctg caggatgact ctctgggcct cctncaaaac cttggccnna anaaccctaa
540agggcgnaat tctgcaaag
559

<210> 56<211> 448<212> DNA<213> Homo sapien
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60ttgtatccat ttcccggggc ttatggaccc attcatactc tccatattta gaatcaaagg
120ttcctttctg aagagacctt aatttttaagg taaaacgtgg tccaagttcc tgaattccca
180ctttcttttc actcctgaat atgtatctgt gaaatctgaa gaatatgtaa tcccggtgat
240tgtggaatgt ggcaacctgc cttccgataa attgaggatt atgaggaaag agagatgcaa
300acatacgtcc aattgaatga cccagccgtg ttgtaaaatt attcagaatt atttcaggna
360tgtgttctgt ggggtccttg cctcttctct taatttcttt accgaagacg aacactgctc
420attttacctc ggnccggacca cgctaagg
448

<210> 57<211> 454<212> DNA<213> Homo sapien
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60tcccccaaac actggatttc taaatcagta ccatgaacca catgaagaac taatagggaa
120gattcgaaac cactaaaca agaggtaaac aagatcagat aaataaaaaa aaaaggntta
180aaacagactc accatattta caattcccat taaattacnc ataaataaat atntacagag
240acgtgaacac tgattccctt atataactgc naatcgtgtt gccaganaaa gttcaagttg
300gtcgttttac cttaaagagg aaaaacttct acaactgaag acatgacatg gaacttcgng
360tatttgtgtt caagtttatt cacaatactg ataaaaagggt ncggcatcat ctttcggctt
420tttttttaag nattggctac aatcttgact gaac
454

<210> 58<211> 364<212> DNA<213> Homo sapien
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60tattccact gtcattgcta gaagaggagg acagtcggga cttcttagag gccagggaca

120ccccactccc ctgtaacttg cctgtctcat catcgctccc agtcacctca taatgacctt
180tgctctttga cccaatcca ccaaaggtac cgaatttcag cttcccggtg tttcccttaa
240ctttccacc ttccagcgac acttccccc cttcaaactc cagcgctccc gtcgggggtg
300aagggtccaga gaactctctt tnatcactga atgaatttga acgggtgccgn ggcttcttac
360tttt
364

<210> 59<211> 368<212> DNA<213> Homo sapien

agaaagcatc atcaacatca ccaccagcag cagcaccacc agcagcaaca gcagcagccg
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120attgacctga agaatttttag aaaaccagga gagaagacct tcacccaacg aagccgtctt
180tttgtgggaa atcttcctcc cgacatcact gaggaagaaa tgaggaaact atttgagaaa
240tatggaaaag caggcgaagt cttcattcat aaggataaag gatttggctt tatccgcttg
300gaaacccgaa ccctatcgga gattgccaaa gtggagctgg acaatatgcc actccgtgga
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368

<210> 60<211> 440<212> DNA<213> Homo sapien

aaaaataatc attcagggtta ttctaaaatt ttgccataaa attagcaaag tatgccttct
60gttaattgct aaaaccaata ttccacatat aaaagcatgt gatctcattc tacatgcagc
120tccatttctg aaaattaaaa acctatcatt tcatgggcta aattatagaa ctttctatat
180tcgaagaact acttcataag actgttatga caaatgcttt ttattacata atatttagta
240gtcatgctca atcaacaagg tcaacagaag cttgtgaata ttctgctaaa taatctagca
300cactaataca tacacgtttt tcagtgcagn aacattgaaa taatccttgt atnctttatt
360cagcagntc tgcaaaactag ggaataaatt aagatacga cacacaagaa ctttttttta
420cctcggcccg cgaccacgc
440

<210> 61<211> 180<212> DNA<213> Homo sapien

ccatgtgtgt caaagtcagg gaatccctcc tcttgggagc caagaggag tctctcaaaa
60ctagaaggga aagggtgttt ctccacatca atccagcttt ggagacattc tattagtac
120atatgccct tccccaaaa acaacaatga agtgttctgt gtgctaacaa catagctttt
180

<210> 62<211> 462<212> DNA<213> Homo sapien

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60atacagggtcc gaggaactcg tgtctactgc agacgaatgc aattaccca ctttctcca
120tacagaattg ttaggaatg tccactcctt tgggggtgat ttttctctc aagttgtage
180caacattttg tccgtaactg atttcagggc aaacatttct gacatcttc tccagctcan
240tctgccatgc cttggcaatc cagtttctg tcatatgcga gccatccaag ttgatgccaa
300gtaagatttg ccagctcaa agtgaaagng tttgcgtntt ggtatccgga atccctcagc
360cccagtagca aagntttagt nattcacctt tctccaatan gacgtttgtg aacgcctgc
420tgcccttttt gtaaaataaa acagggngcc cntgnaagac ct
462

<210> 63<211> 530<212> DNA<213> Homo sapien

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60ttaatttcag aaggcacctc aaggctaaag gctttttgta cttctttcat caatcaagaa
120gttaacacgc ttttattgct attcaagtag caaaggaaaa ctactctcac aaacttcagt
180tcaacagaga agaatcacca ttaagattga gatattggaat tgactaaaac cgaagtctcc
240atacacgtta tcaatggagc aactttcctg tgtgctttca aattaatgaa atcgtgaaag
300aaaagtcacc attogccatt gtgatgttaa tgtgtcattg aagatttcag ttactacact
360aggcactgaa gtaccattct ggaggctgt ccactgtata gaacatttat gaatagaagg
420taaggacact ctgatgattc ccacgaacta ngaggattgg cggtagggtcc ttagatagag
480cttctaacca tgccatgtan agagcactag acacagccct tttcttgcaa
530

<210> 64<211> 478<212> DNA<213> Homo sapien

ctgttgatgg caatgtccgg gaccagggtg aggtggcatc atcggggggtc cctggggccg
60gaggggctgg cctccgatga agttgattga ttgaagttgc agatcccat ccacttgag
120gtgggtgacc atctgtaggg gaagccngtg cccgtactca tagaagggat ttccatttac
180caccaccttg tantgtcag ccaggactat gaagaccagc tcaaaggcgg caccctttt

240gaagggcatg ctctctctcc tctctctcgt gccccacttc cggccctgca acgtgttgaa
300gaccaccttg ttcccaccg tcaaacnncn tgattgaang tgnaatgctn acntntgagc
360ncngatcctg cccaaccaca aaaggttcacg aagaaccctt tcatgttgct ncntggacct
420ctgncnncac cccctaang gcgaattctg caaaaatccn ttcacactnc cggccctc
478

<210> 65<211> 433<212> DNA<213> Homo sapien

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60atctggagtc tctgacagac aaatctaagg agctgccgtt atactgttct ggggggttgc
120gggtttttctg ggacaacaag ttgaccatg caatgggtggc tttcctggac tgtgtgcagc
180agttcaaaga agaggttgag aaaggcgaga cacgtttttg tcttccctac aggatggatg
240tgagaaaagg caagattgaa gacacaggag gcagtggcgg ctctatttcc atcaaaacc
300agtttaactc tgaggagcag tggacaaaag ctctcaagtt catgctgacg aatcttaagt
360gggtcttgc ttgggtgtcc tccaatttta taacanatgn cttntttctt anggggaggc
420tgncttatan gat
433

<210> 66<211> 517<212> DNA<213> Homo sapien

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60caacccctcc agtcaatact ttttcttaat gtctgcattg taatttagca tttgcatgn
120gggagtacac aaatgaattg aatattggat cagaatttac cctaacttga agagtaaaaa
180gttatcaaag ttccacctta catggcttta ttgaaataac attccatcga aaattccaat
240aaaaattgga atatattatg agcaactgcc attgtcatt ttgtctgata ttaacagatt
300atgcatttcc tcagagaagc agtaggnccc atatatacag acatatatat ggctctgggt
360tgaaagagaa gacaaatcct cgtontactt ntatggattt atcactggcg cttntcnaic
420cgaaaaancc aaggttacga cctaccagtt ggaacaacnt tganagggga anaaattttt
480tacctgcccc ggcggngccc taatggcgga ancctgg
517

<210> 67<211> 558<212> DNA<213> Homo sapien

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60agaagttggc tggcttccca ccattaagga aaatgatatc acaagtagcc atggcgagcc
120cagcaccatt cacaagcag gcaatgttcc catctagtcc tatgtatttt agatcatatt
180tggcagcttc attttcaatg ggctcattct ctgatttgct gtccatagca aatatgtctt
240tttgtcggaa ttctgcgttg tcatcaaagt ttatcttggc atcaaaacag acaactgtc
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558

<210> 68<211> 347<212> DNA<213> Homo sapien

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60aggatgaggt ggaacgtgtg atcaccatta tgcagaatcc acgccagtac aagatcccag
120actggttctt gaacagacag aaggatgtaa aggatggaaa atacagccag gtcctagcca
180atggtctgga caacaagtc cgtgaagacc tggagcgact gaagaagatt cggggccata
240gagggtcgcg tcacttctgg ggccttcgtg tccgaggcca gcacaccaag accactggcc
300gccgtggcgg caccgtgggt gtgtccaaga agaaataagt ctgtagg
347

<210> 69<211> 349<212> DNA<213> Homo sapien

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60gccatgac aatcttgag atgggcaagt ctggctggga tttcttcaca ctgttactct
120tctctatgga gcggtttagg gactcgttcc tgtcgatgag ttgtgtgta agggctcagg
180ggaggcgagc tctgttcgat ggtccctcc aagaccaagg ggctgggtgt cctgggctgc
240tgacatttct ggtgtcctc ctgttctcc tcagccctg cggcccccag gttgtcctg
300acagtgtcct ctgggcctgg ccctccttg ctacagactca actcctcca
349

<210> 70<211> 530<212> DNA<213> Homo sapien

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60ggggcaccga gaagtcagca cacatactgc tgggaccagg actcgtaatt cgccttggtc
120caactccttc tatgggttta gctgccctca ttctgtggg taatacaaga tcaaacagtc
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240actgaccagt acagtttctc ctgaattgac aaactgaact actccttcta cgggctaacc
300cctgacatca gtagaatcaa accaaaaaca aggtagagtg ttccacagag aagtgggtga
360ttgaataagg cagcagaaac acataccatc cagccctga acctgaattt tggcnaaaca
420gagatacttt aagtccattt cttttcaaa ggggtntaat gctcanagt ggnaatagng
480actagggtat tctaancggt tgaataataa tntctnagaa aaggttattg
530

<210> 71<211> 484<212> DNA<213> Homo sapien

aaaaacatgt tgaatcatgc ttctttcaca cttattttaa gagagatgta aattttgttc
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120gtctgtctaca tttttgtctc catccatttt tctaccacc tctgaagge tatctgatag
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360ggccagaatt tatgatttta gatcaccttc ttggaaacct tagatcactg tgttttgaaa
420tcatgagttt gcttttaact tcatagggtc aactttacct gccgcgcgg cccgctcgca
480aggg
484

<210> 72<211> 325<212> DNA<213> Homo sapien

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60ggcttctggc tgcacctctt gggttggcag atgatgccac ttccacctc caggcagaca
120cagttcttgc agtcnaactc taagtgtctc ccaaactctc tgggcacatt gtnangtccc
180acacagccgc aggtcttcac gcagacatca aagccaggag cgtagtcat ggtgccctca
240ngacaaaagc agccttccac cangactgtg ttgttctgct gggaggagct ggatttncac
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325

<210> 73<211> 255<212> DNA<213> Homo sapien

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60ctcactgaca tccaggagac ccgcaggcag cctatgccc accctggcct gatgccctg
120cctgacactg ctgcagactt ggattggtcc aacctggtag atgctgcaa agcctatgag
180gtccagagag cctcattttt tgctgctagt gatgaaaacc atcgccctt gagtgtctga
240tccaacagt atcag
255

<210> 74<211> 244<212> DNA<213> Homo sapien

ctgaagatgt tgaagtacag gagatacggc ttatctttgt tctccccat gccacagtag
60gccccagtag agttcctggg gtagaggact tgccgggggt ctccatacaa ccaggccaca
120atccccacca cgatgtaacc tagaatgaag agcaggaaga ggacgcagca gatgacatct
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240tagg
244

<210> 75<211> 575<212> DNA<213> Homo sapien

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60gggcttagtg tccaaactcc tgcccagcct tccctttcca agttggtgcc acctccaggt
120agccattggt ggttttctta ttactgatgt ggctgtggaa tgataaggte ctagaggggc
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420aacagnccac aagtggccaa taccgggact ttgtttcaag ctttttacc tctgccgtga
480cgncgntaa gggcgaattc tcgcnattt tcatnacac tggngggccn ntccangcat
540gcatntaga gggcnccant tcncccttat annng
575

<210> 76<211> 301<212> DNA<213> Homo sapien

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60gcttcaagct tttccttatt ggctccagaa aattcaccca cttttgtcc cttcttaaaa
 120aaactggaatg ttggcatgca tttgacttca cactctgaag caacatcctg acagtcaccc
 180acatctactt caaggaatat cacgttggaa tacttttcag agagggaatg aaagaaaggg
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 300c
 301

<210> 77<211> 335<212> DNA<213> Homo sapien
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 120gcatgagtag cattgatttt ggaaacttcc cagtcgtttt gtaagcttcc actgcccagg
 180gaaaatgtaa aatgggggacc ccgaaataag tgctgatcat catcagtagc ctcaaaaatg
 240agacttccag gtgcactgag gggatggcag aagaacaagc ccgtgtagtc cttggctagc
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 335

<210> 78<211> 223<212> DNA<213> Homo sapien
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 120cttcaacttt tctctttagt gttctgtttg aaactaatac ttaccgagtc agactttgtg
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 223

<210> 79<211> 561<212> DNA<213> Homo sapien
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 561

<210> 80<211> 433<212> DNA<213> Homo sapien
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 120ggagatgtcg ctggggtaga agcctttgac caggcaggtc aggctgacct ggttcttggt
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 300ctccttgcca ttcagccagt cctggtgag gacggtgagg acgctgacca cacngtacgt
 360gctgtgtac tgctcctccc gcggctttgt cttggcatta tgcacctnca cgccgtccac
 420gtaccagacc tcg
 433

<210> 81<211> 570<212> DNA<213> Homo sapien
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 60gttcattgag gatgtcagca gggagtgtt ggaggagttc atctggccgg ccatccagtc
 120cagcgcactg tatgaggacc gctacctctt gggcacctct cttgccatgc cctgcacgc
 180ccgcaaacaa gtggaaatcg cccagcggga gggggccaag tatgtgtccc acggcgccac
 240angaaagggg aacgatcagg tccngtttga gctcacctgc tatttctggt ccccccagat
 300aaaggtoacc gtccttga ggatgccga gttctacaac cggttcaagg gctgcaatga
 360cctgatgaaa taggcaaagc aacatcgggt tccattcca ttactcccc agagtccgtg
 420aagcatagac gagaacctcn ttgcctcatc agctatgagg ctggaatcct tggaaaccca
 480anaaccaagt gcctncaggt ctctacatga agaccaggga cccagccnaa gccctcacca
 540ccccctgaca ttctcgagat cnngttcnac
 570

<210> 82<211> 567<212> DNA<213> Homo sapien
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420ctgatctcca agggtcacaa attcccaacc atcatcatca ctcattttt ccatgtcttg
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567

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420ntaccgatc tatctaaagg gggagcanaa gggggcgga aaggacacaa ttttaacana
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576

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306

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318

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180aaatgacttc tgaggaaagg gaattgtatg catcaatgat caactgaatt acattgctag
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435

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120tatactatgg gaaaccaaga aggaagggga gaaaaaaaag aaaaagcaca gtctatccat
180ccaggacaat cagtaaaaat ctacagtaac ctgatcaacc aaaaatcctt aggtgtgtg
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293

<210> 89<211> 264<212> DNA<213> Homo sapien
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120acctgaactc aggaagaaaa tgcttatctt gatgaaaata tcaacagccc acccacagta
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264

<210> 90<211> 321<212> DNA<213> Homo sapien
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321

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208

<210> 92<211> 201<212> DNA<213> Homo sapien
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201

<210> 93<211> 387<212> DNA<213> Homo sapien
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120tttctctgcc ttctctttt ctctagttc catggtttct ctttcaatca aagtaattaa
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240gaactgagga gagttgcgaa tacactgtcg caattcatca taaacatttt ctttgtcaaa
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387

<210> 94<211> 233<212> DNA<213> Homo sapien
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120tatactagac ataaacttcc cccaccacgc ataattgtat gaaatattta gaattacaag
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233

<210> 95<211> 268<212> DNA<213> Homo sapien
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120gcttgccgtg gcgggacagc atggggcgca atcaccttcc tgttctcctc aatgaggata
180cgcagggtct cgagttggt gaggacagcg tcggcgctca ggctgaagta gaactcacac
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268

<210> 96<211> 178<212> DNA<213> Homo sapien

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178

<210> 97<211> 338<212> DNA<213> Homo sapien

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338

<210> 98<211> 373<212> DNA<213> Homo sapien

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180ttttgagatg gattttcatt cttgttgccc aggttgaggt gcaatggcaa gatctcagct
240cactgcaacc tctaccccct gggttcaagc gattctcctg cttcagcctc ccgagtagct
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373

<210> 99<211> 344<212> DNA<213> Homo sapien

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240ccctttaata ctgcatcatt ctttgggtgt ccctaaatgt tttcagtatt cctataaaat
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344

<210> 100<211> 264<212> DNA<213> Homo sapien

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264

<210> 101<211> 409<212> DNA<213> Homo sapien

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409

<210> 102<211> 185<212> DNA<213> Homo sapien

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185

<210> 103<211> 477<212> DNA<213> Homo sapien

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360acattcctca ttttacattc atttaacctg ccgattattt aattttttta ttgaaagtag
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477

<210> 104<211> 575<212> DNA<213> Homo sapien

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540gatatccatc acatttngc cngtcgaaan tgcat
575

<210> 105<211> 286<212> DNA<213> Homo sapien

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286

<210> 106<211> 410<212> DNA<213> Homo sapien

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410

<210> 107<211> 146<212> DNA<213> Homo sapien

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146

<210> 108<211> 273<212> DNA<213> Homo sapien

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273

<210> 109<211> 264<212> DNA<213> Homo sapien

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264

<210> 110<211> 410<212> DNA<213> Homo sapien

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410

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577

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154

<210> 113<211> 396<212> DNA<213> Homo sapien
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396

<210> 114<211> 344<212> DNA<213> Homo sapien
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240tgccagactg gagtgcagtg gtgcgactg ggctcactgc aatctccacc tcccgggttc
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344

<210> 115<211> 542<212> DNA<213> Homo sapien
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542

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<210> 119<211> 577<212> DNA<213> Homo sapien
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 420acctgctgta cagttttata attgctctta ggtaataatg gtacgctaga tagtatactg
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 207

<210> 121<211> 246<212> DNA<213> Homo sapien
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 120tgcaacttgc tcaaggtga atctcccgag ccgcctttt cctttgcctt tccctgctgc
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 240ctttcc
 246

<210> 122<211> 406<212> DNA<213> Homo sapien
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 120aatgctttt ccaatcattt ctaggggcaa ttttaccct cccatcctga ggcatctgta
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 240agaggtttta tggactcaca gttccacatg gctggggaga cctcacaatc atggcagaag
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406

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120ttggcgaccg atcatgcacc ccttaccatc tcattaaaaac ctaatcacc ctaacccgct
180caatgccaat atctcatccc acagcatgct ttgaaaggat taaagcctgt tatcacttgc
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420ctactaccca ttattctggt ctggatctca aacatgcttt ctttactatt cctttgcacc
480cttcatccca gcctctcttt gccttcactt agactgaccc tgacacccat taggctcagc
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596

<210> 124<211> 255<212> DNA<213> Homo sapien
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120ttatttttctt ttgttgtcca gaatacttat aattctttga gcctcccaga aattggaagc
180taataaaagc aactcaagtt tccttcaaaa aaaaaaaaaa aaaaaaaaaa aanttttnc
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255

<210> 125<211> 332<212> DNA<213> Homo sapien
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120aagaaaagaa gactctgacc tgtactcttg aatacaagtt tctgatacca ctgcactgtc
180tgagaatttc caaaacttta atgaactaac tgacagcttc atgaaactgt ccaccaagat
240caagcagaga aaataattaa tttcatggga ctaaataaac taatgaggat aatattttca
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332

<210> 126<211> 405<212> DNA<213> Homo sapien
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240aatgttgggg gcgggggttc ccttgatgta gtgtggtgta gggagtgtgc ctgtgatgt
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405.

<210> 127<211> 582<212> DNA<213> Homo sapien
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420aaattgatct tcgacctgtt gtgaatcatg tgacttttga caagatgtcc tgctgccaat
480gctgccataa gtgacaattc cccagccatt acggtccac acacaattcn ggcaagctgc
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<210> 128<211> 317<212> DNA<213> Homo sapien
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120ggtgtggctg caccocagca ccgggagggg gcacgcancg acaccagagg aaggacagc
180cccacccatg tcaacagcag gcaacctgtg ttttcatttc aagtgggata cagtattttt
240ttaataagga gccatacttt ttttaagag tttgagatct gaatgtgatt tctaatttga
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317

<210> 129<211> 582<212> DNA<213> Homo sapien

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120tcacgtctc cagggccctc ctggccccgg gcccgaaac gtctgggtca gtgaggtccc
180atctggcagc ctgacctgta tgcgacctg gtcatactcc cgcttggtgg gaggctcctg
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420ctcatcttcc tgtagcngct gtgctgcttg cntgaaaact cttgcncctg tctcctgcgc
480tcggttcccg tccaatgcct ccccntnctc tttttcttca cgctcccgct gcttattggg
540ccaccaantt caacatcctc ttaaattngg nctggtcttt cc
582

<210> 130<211> 116<212> DNA<213> Homo sapien

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116

<210> 131<211> 198<212> DNA<213> Homo sapien

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60tcaagtactt ctccagtctc agcctctgag tagctgggat tacaggcaac caccatcacg
120cctggctaatt ttttgtattt tagtagagac gggggtttca ccatgttggc aaggctgggt
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198

<210> 132<211> 308<212> DNA<213> Homo sapien

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120cagccacctc tgcttataaa aagagtactt agtgacatg actgtaagaa acaattgtaa
180aacctcatct agaaatcaga aagcttctaa tttctataga aatgacacct cctggagcc
240gagagacaat ctgttggtga ttttgaagga caggcaagac caacactgta tttagttcca
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308

<210> 133<211> 262<212> DNA<213> Homo sapien

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120acactcatct gactcattct ttattctatt ttaagtgggt ttgtatcttg cctaagggtg
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262

<210> 134<211> 343<212> DNA<213> Homo sapien

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120tctcaaaaag aaaagaaaag aagactctga cctgtctctt gaatacaagt ttctgatacc
180actgcactgt ctgagaattt ccaaaacttt aatgaactaa ctgacagctt catgaaactg
240tccaccaaga tcaagcagag aaaataatta atttcatggg actaaatgaa ctaatgagga
300taatatTTTTT ataatttttt atttgaaatt ttgctgattc ttt
343

<210> 135<211> 317<212> DNA<213> Homo sapien

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120ttcgtactga gggacacaga cacaggggcc cttctcttca ttggcaagat tctggacccc
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240cagattccac aggacacgaa ggctgcccct gtaaggtttc aatgcataca ataaaagagc
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317

<210> 136<211> 159<212> DNA<213> Homo sapien

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120cgccagcttc ttatcgcgct cgccagcatg cttctttgg
159

<210> 137<211> 264<212> DNA<213> Homo sapien
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120tccattcccg tgggtgtcaa ggcccaggat ggcatacaacc accctgggtg tgtcaaaatc
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264

<210> 138<211> 263<212> DNA<213> Homo sapien
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120actcgcaatt ggttctgaaa ttagaacgtt caccatcgta cttaaaatct taggggcatg
180aagagtcagc tagaacaagg aaaaagaaag tcgcaggtag taggtaagta ggtgggcaca
240tgaaaagcca agctgctctg tcc
263

<210> 139<211> 459<212> DNA<213> Homo sapien
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60aatccagtgt gcagtctgat gaagtctggg tgggtgtggt ctacgggctg gcagctacca
120tgatccaaga ggtaatgcac tccttttccc atctctncac catctgtatc ctggcccaga
180aaacttctc aaccaccaa tttcttcaag gcataaccca atgccatctt gtccgtctat
240aaagcctccc atttttccct ggtatgcatt ccagctcctg ccttcagggt tctgtctgtg
300ggtcatagtt atctctcca cttgctggga gctccttgaa ggcaaagact ctactgcctc
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459

<210> 140<211> 576<212> DNA<213> Homo sapien
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360cacagtcccc atctgcgcag gtccattgtc cactccaag tcaatcaggg ggcaggctt
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576

<210> 141<211> 386<212> DNA<213> Homo sapien
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60aacacataca ctccacctaa caggaagaaa tgccacact atttctatat attcgtcat
120ttctttagaat gggcaaacac ctttctgtaa aagctatata cttttccact cttttcataa
180taaacacttg atgcattcta tccgtcacat tatttaatca gggacaaagt acctatatta
240tatgattcca aattgtgtga ggaaagtaaa aggctaacac tgaaaaataa ctagcatact
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386

<210> 142<211> 227<212> DNA<213> Homo sapien
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60gcccagagcag atgccaacac agcagccatt caagcaatcc tatacaaccg tatcggcgat
120atcggtttca tcctgcctt agcatgattt atcctacact ccaactcatg agaccacaa
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227

<210> 143<211> 246<212> DNA<213> Homo sapien

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120tggaagancc ttgnncttgg gaccggacac ctatggnttt tggcccnngg agggagaaaac
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240acgtgg
246

<210> 144<211> 318<212> DNA<213> Homo sapien

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120attcagggga acctttcanc tattaaaaan nontccaaca anaactcctc accttcgtc
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318

<210> 145<211> 295<212> DNA<213> Homo sapien

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120aatgccaaag gttccccaag ctctttntta nccctngggc naagganggg gcctaattng
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295

<210> 146<211> 147<212> DNA<213> Homo sapien

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60agtctttttt tgcactgttg aaattgggt tggcactcaa gtcaaagatg aacatcgga
120taacaaacat tgtcctctnc aaaaagg
147

<210> 147<211> 69<212> DNA<213> Homo sapien

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69

<210> 148<211> 671<212> DNA<213> Homo sapien

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<210> 149<211> 401<212> DNA<213> Homo sapien

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401

<210> 150<211> 221<212> DNA<213> Homo sapien

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221

<210> 151<211> 142<212> DNA<213> Homo sapien
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142

<210> 152<211> 626<212> DNA<213> Homo sapien
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626

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143

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141

<210> 155<211> 152<212> DNA<213> Homo sapien
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152

<210> 156<211> 335<212> DNA<213> Homo sapien
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335

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420ctcgaccctt atgcttctgc ttttcttga tggtttcgac agtaacattc tttcctttct
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551

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339

<210> 159<211> 385<212> DNA<213> Homo sapien
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120actcccgcga ggntggncct acctcancc tgtctttgga agctagtatg taagtaaggg
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240ctgagtcocct ggcttgttcc agagccctgg cccttgagcc cctggactgg tcagtgcag
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385

<210> 160<211> 147<212> DNA<213> Homo sapien
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147

<210> 161<211> 176<212> DNA<213> Homo sapien
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176

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148

<210> 163<211> 237<212> DNA<213> Homo sapien
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120ccgtctgaac tattctgncc ngcattantc taagtentaa tgggccctcc attccctacg
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237

<210> 164<211> 337<212> DNA<213> Homo sapien
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120acagtacact ggcaactntt naaactnttg nttcttgggg gcttnttcc aataacatca
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337

<210> 165<211> 220<212> DNA<213> Homo sapien
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220

<210> 166<211> 739<212> DNA<213> Homo sapien

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120agctcctgac ncaaggaatg gagggctcnn acctcccnng ggggaaaaa cnggagtg
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360nggtaaacca gcagcttttc cttcganaaa gaaataccat caaantacct tctaaaagct
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739

<210> 167<211> 290<212> DNA<213> Homo sapien

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120tttattaatt ctatttaatn aaggaaaaaa acnttnagaa tccataangt ttcagtttat
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290

<210> 168<211> 250<212> DNA<213> Homo sapien

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120gtgaagaaga aaaacnaaga aggggaaggg aaccacaatt tatntttggg agtttttact
180ggcactgctc caggacaagg ctacttgtcc taaatacatc aagtggaccc agcgagagaa
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250

<210> 169<211> 146<212> DNA<213> Homo sapien

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146

<210> 170<211> 292<212> DNA<213> Homo sapien

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120gaaaaagaaa ggattctcta ttccctgnt tttttttcn cttntatgga cnatatagtt
180tctttttgta agatgcattc attctgacta ttottaccag catttattct tactagcatt
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292

<210> 171<211> 151<212> DNA<213> Homo sapien

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151

<210> 172<211> 131<212> DNA<213> Homo sapien

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120gaagcgttca t
131

<210> 173<211> 90<212> DNA<213> Homo sapien

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<210> 174<211> 472<212> DNA<213> Homo sapien

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120ccatttacc accacaggta ggttggttc tgaacctcag gttcacagg gaagggcaca
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472

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752

<210> 176<211> 224<212> DNA<213> Homo sapien

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224

<210> 177<211> 294<212> DNA<213> Homo sapien

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120tactatttga tatggacctt ttgnttttg gtgaaaactn caaagtaagg agacactgtc
180aatcaattcc actaaaattg catttatttt cctgtcatag taaaaaagga aaacagtag
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294

<210> 178<211> 142<212> DNA<213> Homo sapien

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142

<210> 179<211> 366<212> DNA<213> Homo sapien

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366

<210> 180<211> 104<212> DNA<213> Homo sapien

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<210> 181<211> 393<212> DNA<213> Homo sapien
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393

<210> 182<211> 311<212> DNA<213> Homo sapien
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240tctgtctgcc acaaactcaa tgtattgctt cattagagtgc caattcatcc caatgagctt
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311

<210> 183<211> 277<212> DNA<213> Homo sapien
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180aaaatttttat tagtttgccc aaaccaacat cacttcgaa cntttnttc catcaagtc
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277

<210> 184<211> 322<212> DNA<213> Homo sapien
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322

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358

<210> 186<211> 161<212> DNA<213> Homo sapien
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60cggctgcttc accgggttat tttataaaag aggaagaaaa aaaataaaag totccggcgg
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161

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408

<210> 188<211> 195<212> DNA<213> Homo sapien
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195

<210> 189<211> 134<212> DNA<213> Homo sapien
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134

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125

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120ggccatcaag ggtatgcata tncnaaaaa ncccaaag
158

<210> 192<211> 114<212> DNA<213> Homo sapien
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114

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147

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214

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120cattcgagga gtgccaccg aagtgaagg agctgtttcc cattcagatg gaggtgtca
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296

<210> 196<211> 586<212> DNA<213> Homo sapien
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586

<210> 197<211> 492<212> DNA<213> Homo sapien

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180ganaacaaca ncaacaaaaa aatcanantc tgcagggggc ttgaaaaanc aggagtctnc
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492

<210> 198<211> 414<212> DNA<213> Homo sapien

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414

<210> 199<211> 361<212> DNA<213> Homo sapien

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360t
361

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<210> 202<211> 55<212> DNA<213> Homo sapien

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55

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120atagagtcat catcatcttt gttttccaca ggctttacgg ttttggtagg aagagctgat

180cttatttttt tctcaacagg acgagtttca ggggttgact ggttctttgt gcttccggaa
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398

<210> 206<211> 381<212> DNA<213> Homo sapien
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381

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210

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370

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120ctcgcatgac cggtagctc taaagacaaa aggacctggg tctgcatttc ccaaaggcaa
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278

<210> 210<211> 346<212> DNA<213> Homo sapien
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 283

<210> 212<211> 222<212> DNA<213> Homo sapien
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<210> 218<211> 370<212> DNA<213> Homo sapien

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 332

<210> 220<211> 240<212> DNA<213> Homo sapien

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 120acaccactgt ccccccacgc cgtctggta aaggtcaggt cagcatttcc ggtgatggta
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 240

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 381

<210> 222<211> 636<212> DNA<213> Homo sapien

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636

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120tagagcgatg ataagaatta gcggaaaaaa tgcatgtcag tcgcttagga ggagactggc
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235

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368

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221

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374

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317

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366

<210> 230<211> 330<212> DNA<213> Homo sapien

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240ntttctacaa cttagtctca gcgataccca ttgtatttag ccatgttcaa caacaagtgt
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330

<210> 231<211> 206<212> DNA<213> Homo sapien

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206

<210> 232<211> 468<212> DNA<213> Homo sapien

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468

<210> 233<211> 508<212> DNA<213> Homo sapien

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508

<210> 234<211> 216<212> DNA<213> Homo sapien

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216

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412

<210> 236<211> 214<212> DNA<213> Homo sapien

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60gccgaagtct gagaagtggg tcaattgtga ctggatcatct actggcagtt ataactcaaa
120ccggggacaat ttttatgcta catcagaaaa gaggatnagg aaacagtttg ataacaaatt
180tgttgaatca gaaagcattc ttncactttc attt
214

<210> 237<211> 176<212> DNA<213> Homo sapien

agctcggatc cctagtaacg gccgccagtg tgctggaatt cgcccttggc gccgcccggg
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120cagtgctcctt agattgatat tgatcacatc tttttttttt ttttttncnn aaaggg
176

<210> 238<211> 526<212> DNA<213> Homo sapien

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120tgtgttccc cgcaaaggac tatacatggc aaatgactta aagctcctga gacaccatct
180ccagattccc atccacttcc ccaaggattt cttgtctgtg ggtgcttgaa aaaagaagt
240tgtctgccat gcgtttcctc accgccatga acttgagca tccagagatg ctggagaaag
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360gcatcctggc gntgcagag aaggctggtg tgtctgcaga acaagcccag ggacttctgg
420aaaagatcgc aacgccaag gtgaagaac agctcaagga gaccactgaa gcagcctgcn
480gatnccggagc ctttgggctg cccatcaccg tggcccatgt ggatgg
526

<210> 239<211> 411<212> DNA<213> Homo sapien

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120tagttcattt agtcccatga aattaattat tttctctgct tgatcttggg ggacagtttc
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240agaaacttgt attcnagagt acaggtcaga gtcttctttt cttttctttt tgagatggag
300tcttgctctg ttgccagact ggagtgcagt ggtgcgatct gggctcactg caatctccac
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411

<210> 240<211> 319<212> DNA<213> Homo sapien

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120cgacagggtt ttcccatcat ctttcacggc gtaattggga aagatgagcg tgaaggcaac
180agcccatcct tcttcaaccc tgaagaggct gccacaagt acttctacc tgaagctgct
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300ctcccgtac cggaacag
319

<210> 241<211> 97<212> DNA<213> Homo sapien

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97

<210> 242<211> 190<212> DNA<213> Homo sapien

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60tggcngggcn ncgaagtngc ancgagagg ngantngc cctataccga ncncaagtac
120aattgactg gccgccgcnt gacaacgtgg ngaggccaca gcanccttgt cctccacggg
180gttggagtgg
190

<210> 243<211> 376<212> DNA<213> Homo sapien

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60cgggcangtt tggataacat ttgtattact acaaagttgt tottccctggc tttgtgaa
120ccagtaaagc aaactcaaga ttgagcctcc atgtaatgaa ttggggtaaa gaaaaaacat
180gcaggtcaat aggttaggtt acaaagggtt gtacacacat ttatgacagc aggtcctnaa
240ctgccaacac ctctaaccat ctgattaggt ttctatgagc caagtcttac atattccatt
300catcatgacc ttttagtcaa ttagcaaca gggattccaa cattttgcta aggaatggcc
360cgctaggga actttt
376

<210> 244<211> 405<212> DNA<213> Homo sapien

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120cacccatgaa ctcaccattc caaataactt aattggctgc ataatcgggc gccaggcgcc
180caacattaat gagatccgcc agatgtccgg gccccagatc anaattgcca acccagtagg
240aaggctcctc tggtaggcan gttactatca ctggctctgc tgccagtatt agtctggccc
300agtatctaat caatgccagg ctttctctcg agaagggcat ggggtgcagc tagaacagt
360taggttcctt caataacccc tttctgctgt tctcccatga tccaa
405

<210> 245<211> 312<212> DNA<213> Homo sapien

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60ccgggcaggc ccaaaggta tgatggcagg agtaatcaga ggtgttcttg tgttgatga
120aggggtgaga ggttaaagga gccacttatt agtaatgttg atagtagaat gatggctagg
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240gagtttgatg ctcaccctga tcagaggatt gagtaaacgg ctaggctaga ggtggctaga
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312

<210> 246<211> 634<212> DNA<213> Homo sapien

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120tagattgtat aaggcttgac agaccatagc aagataagca agaactgtgt cctgttaacc
180atttatccct aacatctagc atagagttca gttagtataa gccataaacc ctttgagtct
240tctggcaaga taagtaatta gcacagatta ttgtcactca ctgcaactca gccttgagg
300gagtacacaa atcagaagga ggtcaagtgt ctgggaaatt aaatgacggc acctgcaaga
360acagatcatt gttggggtaa gaaatggaag cccagngtag aaaaggatag aatgccatgg
420ggttagaggt agcagaggct gggacagaac ttgtctgttc tgcccccttt caccctctct
480gttctttgcc ttatgtccaa cccatcactt gctggggtag tcagcctagt tgaacagggt
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600gtcactctgg tgaacacag attctnactc agag
634

<210> 247<211> 325<212> DNA<213> Homo sapien

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60cgggcaggct cgggcaggta aaggcagaca ctgagtcagt attaatagat taactaaact
120gcaactgta ttagataaaa ttactgtgtc tcaactgtga ttacatgcaa aatccacata
180aattgtcatt taaccaacag tactgcacga gcgaacatct cgtatatga aaactgcac
240atcaattcaa cgttttggtta cttgaaactg catcataaat gcaacattgt catatgtgaa
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325

<210> 248<211> 638<212> DNA<213> Homo sapien

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120actaatgaag gctaagcaga atagtctgag ttgtctgaga ctaaagcagg gatagtgttg
180aaaagttttc ctttcaactag tgggacacat tccccttttc ttttcaaga ggaagaacat
240ggtgtcatcc aatgtgaagt gagcagtttc gggcctaaact cttatggtta gaaactaaaa
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360ctgatcatta aaacagagac acctcactg gtgtccaata aggattctct ttacaaaaca
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480ncagcagact gggtttctat tagaacaagt atcagcaagg tcatgtagac ttgtagaaac
540ttttgccttc tctgtcacca gacagatcat tgtccagacc tgcccgggcg gccgctcaan
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638

<210> 249<211> 178<212> DNA<213> Homo sapien

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60gccgaagtct ggctcttga gtctgtggg ggaccccaaa gttggtggc ccatagcctg
120ccctcctggg tctccacctc atgcctggac aggacgctgt ggctgtccg ggccttgg
178

<210> 250<211> 477<212> DNA<213> Homo sapien
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60gccgaagtct gagagncag gngaagttcc ngatgcagng actgtgatgc tcttgactat
120ggaattattg cggccagtag ccaagttaga gacaaaacag gcataggtcc cgttattatt
180tggcgtgatt ttggcgataa agagaacttg tgtgtgttgc tgcggtatcc cattgatnccg
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477

<210> 251<211> 561<212> DNA<213> Homo sapien
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120tcccgcctcct aaggcaggaa gatggtggcc gcaaagaaga cgaaaaagtc gctggagtcg
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561

<210> 252<211> 284<212> DNA<213> Homo sapien
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60cagaggccat ctccattgac acagcgtgct cagcagagac aaccaagaac ccgtcacttt
120gagcangttg agtcttattt gttttatttt gtcctatagt actcttcage agtgcaata
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284

<210> 253<211> 656<212> DNA<213> Homo sapien
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540ctttaacatc gaggatggaa cttnngcgcg aacactctaa ggcaattcc accnccttc
600gccgtactag tggatcgact tcgtcccaac ttggcgtatn tggcntanct gtttc
656

<210> 254<211> 190<212> DNA<213> Homo sapien
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60ctccagcaac aactccaaac ccgtggagga caaggatgct gtggccttaa cctgtgaacc
120tgagattcag aacacaacct acctgtggtg ggtaaataat cagagcctcc cgtcagtc
180caggctgcag
190

<210> 255<211> 446<212> DNA<213> Homo sapien
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300tatganattt gcggaacgcc gtggtggggg gtaaagggca ccaaacctcg gccgcgacca
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420caaaactnnggc gtaacatggg cataac
446

<210> 256<211> 315<212> DNA<213> Homo sapien
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60gatgttcttg tagtccagcc acaggatgtt ctggtcacac ttttcatgt aggcgttatac
120cagccgtgat ttttgagagt ggctcccttc ttcagctcca cctctgcagt gccgctgccc
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300ttcccatcac accag
315

<210> 257<211> 524<212> DNA<213> Homo sapien
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60ttcccagaat ccaccaccgt tactagaaag ctgtcaaagg cattctccga tgccatccag
120gaaactgtga acccgtaggg attaatgtcg gaaatggta ggttttccag aaggggcagg
180gcctctgtcg tggctgtggc actgatggtt ttggtccgga tgctgggagc aagtccagag
240aggtagacaa taaaatcagt actaggggt agccctgaga tatgggcagt tcgttcagca
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360aagtctctga agatcccatc ngtagccatc caggagagat tgaagctttt cgggagttat
420gtcagaaaca ttttaagtttc caatttcagg ttctttggct gtggaggact tgcccgggag
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524

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60caaggcatga gagggaagt ttgttggtga cagatctgtg cctactttat tactggagta
120aaagaaaaca aagttcattg atgtcgaagg atatatacag tgtagaaat taggactgtt
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261

<210> 259<211> 190<212> DNA<213> Homo sapien
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120attatataca tacatgaaac tgcaatttta tggcattcta agtaactcat ttaagtacat
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190

<210> 260<211> 692<212> DNA<213> Homo sapien
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660gaacttggtt ccaaacttgg cgtaatctgg gc
692

<210> 261<211> 356<212> DNA<213> Homo sapien
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60aattatacca aattcctctt atcaactgca tactaagtgt tttcaatata attttttccg
120tataaaaaata ctgggaaaaa aattgataaa taacaggtaa gagaaagata tttctaggca
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240gatcatgctt gttcctacag tattcggggc cagacactta agtgaaagca gaagtgtttg
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356

<210> 262<211> 366<212> DNA<213> Homo sapien
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366

<210> 263<211> 389<212> DNA<213> Homo sapien
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389

<210> 264<211> 409<212> DNA<213> Homo sapien
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240tggctatctg ggacatggta nctgggtgc catcgtcaaa ctctaagaca tctgtgtaga
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409

<210> 265<211> 161<212> DNA<213> Homo sapien
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120tgacaccatc atgtaaggag ctggctgacc tcatgaccg c
161

<210> 266<211> 455<212> DNA<213> Homo sapien
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455

<210> 267<211> 261<212> DNA<213> Homo sapien
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120gggacttggt tanagagcct gtcaccagag cttctctggg ctgaatgnat gtcattgtgt
180ataaatgcca gagccaacct ggacttctg tcatcttcac aatcttgggg ctgatgaaga
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261

<210> 268<211> 111<212> DNA<213> Homo sapien
ccacagcagg actacagtca agacaatcac agtctctgcg gagctgccca agccctccat
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111

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 240gctgactgtg attcttaaat tgagaccaga gcagcaaacy tctcacttt
 289

<210> 270<211> 538<212> DNA<213> Homo sapien

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 538

<210> 271<211> 220<212> DNA<213> Homo sapien

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 120gcacctctaa gatactgatg gctctgcaga ggacccattc attgcttctg cttttgctgc
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 220

<210> 272<211> 238<212> DNA<213> Homo sapien

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 120tctagaaata tacatagaca agtttagcta atgaataaaa taagtaaaat gactacataa
 180actcaatttc agggatgagg gatcatgcat gatcagttaa gtcactctgc cacttttt
 238

<210> 273<211> 504<212> DNA<213> Homo sapien

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 120gcagcacaac ttgaattat gagcaggacc agaaatactc tttctgcaca gaccacactg
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 240acaacaacca caattacact gattgcactt ctgagggcag aagagacaac atgaagtggg
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 480tgacatgca ttgcctact ccca
 504

<210> 274<211> 388<212> DNA<213> Homo sapien

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 60tgatattct ttgccagat tatggcagac aagttaacga gaattgctat tgtcaacccat
 120gacaaatgta aacctaaaga atgtcgacag gaatgcaaaa agagttgtcc tgtagttcga
 180atgggaaaat tatgcataga ggttacacc cagagcaaaa tagcatggat ttccgaaact
 240ctttgtattg gttgtggtat ctgtattaag aaatgccct ttggcgctt atcaattgtc
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 388

<210> 275<211> 344<212> DNA<213> Homo sapien

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 120gcaggtgggt tagaggctgc atggcaggag aggtgaggt tcaccctgg acggtaatag
 180gtgtatgagg gggaaatggg ggggtcgtct gggccataga ggacattcag gatgactggg
 240tcgctgtggg caacacttaa tttgttctgg attccacact catagggtcc tacatcattc
 300cttgtgacac tgagtagagt gaggtcctg ttgtcattgg acag
 344

<210> 276<211> 418<212> DNA<213> Homo sapien
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60tttagatctta ttcacacagc tgctgaacag ttcctttttc agagacatag ataccatcca
120aaaattttcct gacatccttg tttttaactg ttgtggcttg ctgaatcaaa gccgctgaat
180ttgaaacaag ctcaatgtca tttccttcaa ggattaattc atctttctgg gcttgagata
240ctgaacaagc aacacctggt ctcatccgaa cctgcggat gtatttttca cccaagaaat
300ttcggatttc aacaagagac ccattctcct ggataacaac gttgatggg aagttagcat
360acacagacct catcttgtaa cggaagccca gtgtaacacc cttgatcatg ttctgtac
418

<210> 277<211> 758<212> DNA<213> Homo sapien
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60aataagtggc ttttttctgg gctaccatta ttgtttgatt tctctttgtc aagtgtatag
120aacctgtcat acattcatga taagtagcac tgaaaaatta ctcatcaca tttccctgg
180gcacgtaagg caaatattg ccggttgga tttcaaggc agtgacgacg catttcctcc
240cagtacagac cccccagccc cccttgctgg acatggggag gcagagagtc acttgacct
300ccagaaatac atgactacaa gtctttatg accgtttgcc attttttta atggtactta
360gtattttgat caaactttag tctccagaac taaacaagtc cctaagtttc cttattttta
420tttactgtga ctgatttga agcaataaaa tactccagat ccatgcagct agaacacact
480tgcttncact actaaatata cagggtatgt cctaactatg agttaactgg gaatagcant
540acacttagca agtatctgtg aatncttagc actgaccggg taacaagaaa tgctttgggt
600aatancctac ttanttaatt gggaggaagg tngtaaaaata aacnttaggt aatttgcgna
660atacttcaaa ngggaaaaat ttttttgtgn ancttttagn accctttttt ncctannntt
720gaaaanggn gaantttttg ntngacaatt aaaaattt
758

<210> 278<211> 392<212> DNA<213> Homo sapien
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120tccacatggt gatttaataa agtcagaatg gcagggtgga ggatggtaaa ataaacttac
180caaggggcaa aaggaaccaa acatttactg agtgccgact atgcaagctc tactaggttt
240tacacacttt acataaacgt gaacctaatg tctagttatc agttaacagg ccagcattgc
300tacagccagt aagtctatgt tttcaatgtt ctttcgcttt taagtacaaa ttgtggaaca
360aaactatatac ttgccccaaa gaagcacatc aa
392

<210> 279<211> 88<212> DNA<213> Homo sapien
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88

<210> 280<211> 588<212> DNA<213> Homo sapien
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120ctactgggcc aatgctaaag tttctgtctc taagcctaaa aaagccagt tagtagggcc
180cttatcactc ttagtttctt aggtttcccc tctgaaataa tgagcagatt tagccaggct
240agcagaaagg aagaggacgg ggctgtgcag gagttagcag aatcttgatt cttgctctat
300ggtcggtact tgcacaggaa gtgttgccgc ttgttgcatc cgttgctgct ccaagttaa
360aagtttggtta ttggagctca tctcagcaga gtgcttgctc ccacccatgg acttgccaga
420ccaggatctg tcagatacat ggcccatcat cccttgccct tgctgctttt tttggggctg
480tgaggccaa tccatctcgg ttgnttctnt gatacccctt atgacctent ctttgggggt
540ggnttccttt acctngccgg anccccctaa gggcnatttc cncncct
588

<210> 281<211> 453<212> DNA<213> Homo sapien
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60ttccttaatt tttttttatt tcagtttctc atagagctaa atggttttac atatattctc
120ttgtcagatt tgtggtctaa tagaggtaga aaatggaaat tttccagta cttagaaata
180tggtacttag gaagaagtct aggatgtgaa ttacatatc acttccccta gtgactatga
240taatacaagg ggcagatagc agaggaaaat aagttaacat gaaatttgac aaattttatt
300actttgccaa aattagcaaa aaaaaatac tcacctccc ctgctcacc cccaactttt
360tataaatatt caattcagct acaaaacaaa atactggacc cacttctttc agaagagatg

420aagatacctt atatgcccta aagttaatac cag
453

<210> 282<211> 708<212> DNA<213> Homo sapien

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120gtgcacactg gctatcattg atccagggtga ctctgacatc attagaagca tgccagaaca
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480caacatgggc agcatcacca gacttcaaga atttagggcc atcttccact ttttaccaga
540acggcgatca atcttttccn ttagctnaag caaacttgca ttgcaatggg gaaccgggt
600gggnaattcc aatacagggg cattaccccg gngcttantt tggcctngga nggttcaggg
660atnaataccc cctnnggccg ggaaccncn ttangggnga aatttcaa
708

<210> 283<211> 227<212> DNA<213> Homo sapien

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60gagatctatc tcttctccct gccattaag gaatcagaga ttattgattt ctccctggg
120gcctctctca aggatgaggt tttgaagatt atgccagtgc agaagcagac ccgtgccgg
180cagcgacca ggttcaaggc atttgttgct atcggggact acaatgg
227

<210> 284<211> 478<212> DNA<213> Homo sapien

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120aaatctcctg cctggtagc aatatgtagt gagtgtctcc agtgtctacg aacaacatga
180gagcacacct cttagaggaa gacagaaaac aggtcttgat tcccaactg gcattgactt
240ttctgatatt actgccaact cttttactgt gactggatt gctcctcgag ccaccatcac
300tggctacagg atccgccatc atcccgagca cttcagtggg agacctcgag aagatcggt
360gccccactct cggaattcca tcacctcac caacctcact ccaggcacag agtatgtggt
420cagcatcggt gctcttaatg gcagagagga aagtcctta ttgattggac ctcggncc
478

<210> 285<211> 150<212> DNA<213> Homo sapien

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60gtcaaaagc tttgtgtttt catagagagt ttcattcaca atgcgatcag acttagattt
120gaaaacagct ctaggatac ctgtgccac
150

<210> 286<211> 328<212> DNA<213> Homo sapien

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120gtggaaatga agaaagtaca aagacaggaa acgctggaag tcgtttggct tgtgggtgta
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328

<210> 287<211> 232<212> DNA<213> Homo sapien

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60agggatggga gggcgatgag gactaggatg atggcgggca ggatagttca gacggttct
120atttcctgag cgtctgagat gtagtatta gtagttttg ttgtgagtgt taggaaaagg
180gcatacagga ctaggaagca gataaggaaa atgattatga gggcgtgatc at
232

<210> 288<211> 418<212> DNA<213> Homo sapien

cctctcccag gccatggga cacaggcgag cagcccgttc ctactgagag aggagagcca
60ggctgaccag cacatccggt atggccccc gaataccgat gatgccatct cctcagacca
120ggagagactt catctcctgt ttcccaagtg tgtcatcaat atcatgacct tctcagcat

180cctcatgggc ttgctccaag gggtttactt ccctgccctg accagcctgc tgtcgcagaa
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300gacgctgctg accggggcgg tgggctccct gtcctggaa tggtaggct ggcagagcat
360cttctatttc tccggcgcc tcacctgtg ttgggtgtgg tacgtatata ggtacctg
418

<210> 289<211> 663<212> DNA<213> Homo sapien

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60acatcatcaa gtatgagaag cctgggtctc ctcccagaga agtgggtccct cggccccgcc
120ctggtgtcac agaggctact attactggcc tggaaaccggg aaccgaatat acaatttatg
180tcattgccct gaagaataat cagaagagcg agccctgat tggaaaggaaa aagacagttc
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360ggcgggaccac accgccaca acggccacc ccataaggca taggccaaga ccataccgc
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600gttcaaggg cgaatttcca cccccnttn gngccttact agngggntcc ncnctggn
660caa
663

<210> 290<211> 206<212> DNA<213> Homo sapien

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60ananagccct ggtggccgtc acggtcacag accgggcccc ggtggccgac tatctgacct
120cacagttcta tgccctcaac tacagnctcc ggcagcgcac ggacatcctg gatgtgctga
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206

<210> 291<211> 360<212> DNA<213> Homo sapien

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60ggtcttctgt gcagcctccc atggatcaat ataccagtta gttaaaacac acatcagat
120tttctgtcct ttagcaacga tgatgatatt tgccaccagc gagtgtgato cgtgaggcaa
180ttttggaaac tgacttggtg cttgccacta tcttcaggct tacagccctc agacgaggca
240aaggaggga aatcgatttg agaccactga ttagcaataa cgtatttagc attttgctct
300ggttttgga gataagggtg agttaattat caacatcata ctttccaaag aaagaatttt
360

<210> 292<211> 174<212> DNA<213> Homo sapien

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60gcttgccacc accagatgag aagttaagca gcctttctgt ggagagtga aataattgtg
120tacaaagtag agaagtatcc aattatgtga caacctttgt gtaataaaaaa tttg
174

<210> 293<211> 406<212> DNA<213> Homo sapien

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406

<210> 294<211> 304<212> DNA<213> Homo sapien

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60agctgcccg ccatgctggc tccatcaatg aagtggcttt ccacctgat gagcccatca
120ttatctcagc atcgagtga aagagactgt atatgggaga gattcagtga agatattgac
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304

<210> 295<211> 349<212> DNA<213> Homo sapien
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60tgcagattca ggcgccgtgg tccctgacta aggcactctg cctagatcta ttttcccctg
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240tgactgttga gtggcggctc tttggaattg taatttgaga aggattgtga agaaatcagt
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349

<210> 296<211> 208<212> DNA<213> Homo sapien
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208

<210> 297<211> 218<212> DNA<213> Homo sapien
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60ctcctgggga tgattatgac catggaacag ctcacaagta tatcattcga ataagtacaa
120gtattcttga tctcagagac aagttcaatg aatctcttca agtgaatact accgctctca
180tcccaaagga agccaactct gaggaagtct tttgttt
218

<210> 298<211> 545<212> DNA<213> Homo sapien
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360aatgcctgtt cattcttgtc ttttaattcc ccaagataag cagcattttg tncaaggata
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545

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180agggaaaaag gagaaaatca gatttaagaa gatcanaaaa agaagacnga ataaagaga
240aagcatgtac ctganaaagg cttggaggga aactctaaaa tcagngtcac ttccaaaaaa
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410

<210> 300<211> 545<212> DNA<213> Homo sapien
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545

<210> 301<211> 393<212> DNA<213> Homo sapien
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120gcagggtgggt taagaggctg catggcagga gaggctgagg ttcccccctg gacggtaata
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240gtcgctgtgg tcaacactta attcgttctg gattccacac tcataggggt ctacatcatt
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393

<210> 302<211> 177<212> DNA<213> Homo sapien
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120gagggcagggt ggagagagga cggagaaaac agctaccaa aagggagggg ggagttt
177

<210> 303<211> 413<212> DNA<213> Homo sapien
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240atcgaatggga taaccgagca tcacacacaa gttctcttta tgcgcaaat cagccaaat
300aataacggga cctatgcctg tttgtctct aacttggtta ctggccgcaa taattccata
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413

<210> 304<211> 500<212> DNA<213> Homo sapien
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60aattatcaat gaagtggaca aattcctagg aagacacaaa ctaccaaacc caactcagaa
120gtagaaaact tgaataaacc tatatcaagt aaatagggtt aatgagtttt tgaagagata
180cccacaaaaga agagcccagg ctgaaatagc ttcttaaatg aattctacaa aactttta
240gaaaaattaa tacaattctc tcacaaactt ttcaaaaag tagaagagtgt gtgaacactt
300ctgacacata ctacaacatg gaagaactca gaatatgctc agtgcaagaa gccagtcaca
360aaagactaca tattatatga tactatttat atgaagtgtc cagaattggc aaatatatag
420agatagaaag tggattagtgt gttgcttagg gctagcacag anttgggggg aatgggaang
480gctgggggta acagacctcg
500

<210> 305<211> 434<212> DNA<213> Homo sapien
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240agagatgggt ggcctgccat gggatccat ggtgacaaga gtcaacaaga gcgtgactgg
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146

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120ttggcttctg gggaaaccaa aaatatatta aaaaaggaga gaccaggacc ttaaaaagag
180cccaagttgt tgagctccct gccaaagtcac cccaggtat ctctgccac cagcttgcac
240gagccagatc ctcaagtgcag gtttttccaa tcagtcattt gttcttccac ccaacgctca
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353

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120cggggccccg ccccccaat tnggtggaaa atngggaant tttttttttt tggccanana
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590

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120ttggcctcaa acaatcctcc tgtttcanc taccaaactg ctgggattac aggcagagc
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318

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120atttctctgag cgtctgagat gtagtatta gtagttttg ttgtgagtgt taggaaaagg
180gcatacanga ctaggaaagca catnaaggaa aatgattgtt aaggcgacc tgccccgggc
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120ctaatacaaat atgttgattc atggctataa taaagcagga gcaattataa aatcttcaat
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225

<210> 313<211> 248<212> DNA<213> Homo sapien
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120ccccctccc agaagaagtg gatgaaacca gtgctgaaga tgaagggtgc tctcagagga
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248

<210> 314<211> 345<212> DNA<213> Homo sapien
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120caatcttaat gtctcttcat aatactttta taatacatta agcctcttgt ctacatattt

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240atatatgtat gaaataaaaat tagttccatt tggctttcta gtatatataa gtgctatctg
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345

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120acaaccagtc agagtactcg gtgggttcag aggaggagga tgaagacttc gatgaacgtc
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300aggctttcct caatgctgtg atgcgctggg ggatgccacc acaggatgcc ttcaccacac
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413

<210> 316<211> 88<212> DNA<213> Homo sapien
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88

<210> 317<211> 147<212> DNA<213> Homo sapien
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147

<210> 318<211> 299<212> DNA<213> Homo sapien
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120atttatatta aaaaatagtg caaaatctca acatttatat aaataactct aaacccctgc
180tttgtaattt ttttctttac aagtaatac acactttctg acttggcact caaaaattgc
240catttttttc ctcttctagt tcagaaaaca actttttttt tttaatagga cctcggccg
299

<210> 319<211> 100<212> DNA<213> Homo sapien
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100

<210> 320<211> 325<212> DNA<213> Homo sapien
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325

<210> 321<211> 80<212> DNA<213> Homo sapien
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80

<210> 322<211> 86<212> DNA<213> Homo sapien
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86

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60gcttgtattc ttccattgga taagtagaat ttctcatcat tattgtactc gtcaaatact
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180aacttttttc ctgcaatgag atcaggagtg aggtggatcc tttcacccct ctctccacag
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244

<210> 324<211> 344<212> DNA<213> Homo sapien
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120atcctatac gccaagccc ataactcaga cactggcctc aataggacca cagtcacnac
180gatcacagtn tatgagccac ccaaaccctt catcaccagc aacaactcca acccgtgga
240ggatgaggat gctgtagcct taacctgtga acctgagatt cagaacacaa tctacctgtg
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344

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120gactaccatt aatccaggga gggccaggag gaccttgagc accagcgtgt ccctgaggtc
180caggttctcc tctttgtcca ggggcaccat ttgaaccagg agaccctgca ggtccaactt
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255

<210> 326<211> 335<212> DNA<213> Homo sapien
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335

<210> 327<211> 295<212> DNA<213> Homo sapien
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180acgcctgtag tccagctac tcaggaggct gaggcacaag aatcgctga atccaggagg
240tggagggtgc agtgagccga gatcgacca ctgactcca gcctgggtga cacag
295

<210> 328<211> 417<212> DNA<213> Homo sapien
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417

<210> 329<211> 483<212> DNA<213> Homo sapien
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483

<210> 330<211> 358<212> DNA<213> Homo sapien
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240aatttctcct agaaaaatct gtttagcattt cttaaaagtc cctcagattt gagggaaatt

300ctaaattagg acagntttct ctccaaataa atataaatga tcttgagtat ttttgttt
358

<210> 331<211> 306<212> DNA<213> Homo sapien

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120tgtaaatctg gataactttt aatatctaaa ctatataaga aagtaaaatt taacatgtta
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240aaacacatac ccatctaaat ttttttatag ccttccatgt taaactataa gtaaataatt
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306

<210> 332<211> 251<212> DNA<213> Homo sapien

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251

<210> 333<211> 579<212> DNA<213> Homo sapien

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579

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360cccacaaact ttaattttgt taaatttata tggntttgaa atagaaagta taagttgcta
420ccattttttg ataacattga aagatagtat ttaccatct ttaatcatct tggaaaatac
480aagtcctgtg aacaaccact ctttcacctt ccagcatgag ggcaaaagta aagg
534

<210> 335<211> 282<212> DNA<213> Homo sapien

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120ctgcaccct cgcaatgaga ccagggtgcc ctgctccacc gtcccgtca ccacggaggt
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282

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120tgggtggtctg ggggcagtgc cctctggccc cttcctagca ccaaaaggga ggaattgggg
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193

<210> 337<211> 341<212> DNA<213> Homo sapien

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341

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<210> 339<211> 222<212> DNA<213> Homo sapien
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222

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314

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120cctctttgtt tttttccaag gcccggaac aaaactcatg ctgtgccatc atgtgatgca
180gcctggcaga ggcccaatgc tggaaatgca ccatcattca catcagaact gcagcccctg
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289

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356

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472

<210> 344<211> 446<212> DNA<213> Homo sapien
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120cccatagttg ctaacaatcc tatttaacca ctaagaaagg atttacaaca ataaaagcta

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<210> 346<211> 499<212> DNA<213> Homo sapien
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240ctgtccacca agatcaacca gagaaaatna ttaatttcac gggactaant gaactaatga
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360ccgntaangg ccaatttctc aattccatca cnaactggcg cccgnttcga ncatccatct
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499

<210> 347<211> 539<212> DNA<213> Homo sapien
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539

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69

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120gcatcccctg gcagaggctc ctgctcacag cctcacttct aaccttctgg aaccgcccc
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283

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120agaaccggag gctggagagc aaaatccggg agcacttggg gaagaaggga cccagggtc
180gagactggag ccattacttc aagatcatcg aggacctgag ggctcagatc ttcgcaata
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327

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120gatgggggtg tggggagggg atgagcactc tgcagccgat taatctgttg gtaggggcc
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258

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120tgggaatatgg gcttatccaa cccaaccaag atggagagtg aggggggttg ccctggggcc
180aaggctcatg cacacgtac ctattgtggc acggagagta aggacggaag cagctttggc
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347

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120ttgtgagaac tgctttattg gatgctgctg gtgtggcctc tctgttaact acagcagaag
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240tgggaggtgg tatgggaggt ggcattgtct aactcctaga ctagtgtctt acctttatta
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359

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120ctggtgtcac agaggctact attactggcc tggaaaccggg aaccgaatat acaatttatg
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251

<210> 355<211> 343<212> DNA<213> Homo sapien
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120gtttttgtgg ccttgaattt taagacaaat attctacacg gtatattgca caggatggat
180ggcaaaaaaa gtttaaaaaa aaaaaccctt aacggaactg ccttaaaaaa gcagacgtcc
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343

<210> 356<211> 306<212> DNA<213> Homo sapien
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120gaggtagagg agtagttgtt agagggtgg aagtgggtgg tgggtggaagg gtggtcgtgg
180tggttggttg agggctggga gtggtggttg gtgaaggggt ggnatgggt gtnggtggac
240ctcggnccg accacgctna ggcgaattc cagcacactg gctggncng nctaattgga
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306

<210> 357<211> 357<212> DNA<213> Homo sapien
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120gcaagactct cagacattag ctgaaccaag tgtacacagt cagactgcaa gggcactgat
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357

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120tgcctgtgag gttcacaca attttccag ctctgtgggtc atcaatgatt tcaaattcgc

180caatgtaacc atgcttcac atcacagtga gaaaccggac gatgactttg gagcacggcc
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250

<210> 359<211> 469<212> DNA<213> Homo sapien

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469

<210> 360<211> 313<212> DNA<213> Homo sapien

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120ttctatagat tcttatcttg ctacaggac ttgctccaaa actgaatttt cagaagcagc
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313

<210> 361<211> 373<212> DNA<213> Homo sapien

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120gagtaggaac acagacagca gtactgtatc agcaaatct atcatattat ttgaaatcac
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373

<210> 362<211> 536<212> DNA<213> Homo sapien

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536

<210> 363<211> 276<212> DNA<213> Homo sapien

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276

<210> 364<211> 540<212> DNA<213> Homo sapien

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480ataaaaagcgg ccgggtgccg ggggctcacc ctgtaatccc aactactccg gttttnggaa
540

<210> 365<211> 416<212> DNA<213> Homo sapien
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120gcaagggaaa taatgcagtt tcctgtctta ttttaagaaaa agagaaggct ctcttttctc
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416

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120catagtgcct ggcacagaat tactgtctca atgttagctg tcgtattaat attgtcactt
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221

<210> 367<211> 173<212> DNA<213> Homo sapien
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60ggagggttagt tgtggcaata aaaatgatta aggatactag tataagagat caggttcgtc
120cttttagtgtt gtgtatggct atcatttggt ttgangttag tttgattagt cat
173

<210> 368<211> 344<212> DNA<213> Homo sapien
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60gaggctgtgg cactgggtga aaggaggga gaattggagcc tggccctgt gtgtacaaca
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344

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410

<210> 370<211> 541<212> DNA<213> Homo sapien
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541

<210> 371<211> 357<212> DNA<213> Homo sapien
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60ccacacaaaa gccaggtaac attaacaaaa gaattccctg tatcatctgg atctcaacat

120cggaaaaaag aagcggatag tgtttatgga gaatgggttc ctgtggagaa aaatgggtgaa
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357

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485

<210> 373<211> 543<212> DNA<213> Homo sapien

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543

<210> 374<211> 540<212> DNA<213> Homo sapien

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199

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374

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540

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240tctcggataa ccagctgcaa gagggcaaga acgtgatcgg gttacagatg ggcaccaacc
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368

<210> 379<211> 542<212> DNA<213> Homo sapien
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344

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496

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120cattttataag tgatcagtta atgcctaaga gtgaaagtag ttctattgac attcctcaag
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<210> 384<211> 218<212> DNA<213> Homo sapien
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218

<210> 385<211> 100<212> DNA<213> Homo sapien
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100

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548

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207

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351

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264

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72

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510

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120cccagctatg gagatattaa tacattgatt caaatcccat tactcaatcc acatagccct
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240tgatgttata caagtcaaac ttggaagggtc atagtaagca tacctatgct gagagaaaaag
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374

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316

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<210> 404<211> 326<212> DNA<213> Homo sapien
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412

<210> 412<211> 365<212> DNA<213> Homo sapien

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365

<210> 413<211> 386<212> DNA<213> Homo sapien

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185

<210> 415<211> 342<212> DNA<213> Homo sapien

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286

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522

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421

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279

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526

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303

<210> 428<211> 365<212> DNA<213> Homo sapien

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76

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527

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284

<210> 446<211> 532<212> DNA<213> Homo sapien
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250

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<210> 474<211> 559<212> DNA<213> Homo sapien

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 360cantcntaca taaatanttt tnaagtggaa cctaattaac ctattaataa ttaatgaatt
 420aatttttaagc atcaaatatt gggcncgaat ttgggaaaaa tnaagnatg aatccttggg
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 180ctatcttaac tgctgaagaa tgaaaaacaa aatgacccca gatttttcaa ggtcaagtat
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 240ttatgtaagg ttttttttgc acgcaattct cgattctttg aagagatgac aacaaatttt
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360ataaaagtgc tgccgtaaaa aaaaaaaaaa aaaaaaaacn tgggcc
406

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120aagtcttccc ccacgtccc ccaatgggg gactatgggt tactgtgatc aagagacacc
180tgaacataaa acacaactac acttctacca aaatcaaact caaatccaca caacaaaaca
240gaattgagca atcttaccag ggattgaaaa ctgagggtgt gagatgctgg gctgagggcc
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386

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120tgggtgtcat ttggggagtt ttgccattac gagggttctt gggaatagca ggattctgcc
180tgatcaatgc aggagtcttg tacctctact tcagcaatta cctacagatt gatgaggaag
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300tggtcatttg gatcatcttt tacactgcca tccattatga ctgatggtgt acagctccca
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420ggaacccccc cccttggaac ttggaagacc cctgttttct ggaccncgaa tcanngtggt
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213

<210> 489<211> 297<212> DNA<213> Homo sapien
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120gtaaatacat ggcttgctgc ctgttgctacc gtggtgacgt ggttccaaa gatgtcaatg
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297

<210> 490<211> 347<212> DNA<213> Homo sapien
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180ctcaggctgt aaaagtagct gagccatcct gccattcctt ggaggtccta caggatgaaac
240tgcaggagct cagcatagac ccagctctct gggggatggt cactggtga tttcaatgat
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347

<210> 491<211> 566<212> DNA<213> Homo sapien
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420tnaatgagaa caattaagac ctgnccccc actgttgctt gaggaatgan gncctttgct
480tttcatgtct ggnatttctt anancctca ttttaccaaa tganagaaac tggaggnttg
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<210> 492<211> 561<212> DNA<213> Homo sapien

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120cacggtggaa acgcttatgt tacatccggg gatcaaggct ttctgtgtg gctccatcag
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360tgtccctggc gttggaatct actttggcac tctctactct ttgaagcagn atttcttgcg
420aggccatccc ccaaccgccc tggagtcaag tcatgctggg ggtgggctct cgtctgttg
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561

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120tgtcttatgt aaataataaa ctaattgtgg ctgttaaagt atttgtatgt gatcctgtcg
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240tgccggaata acaccaaag gaatctctc atctcttgct tgttagcgat gtgtctgatt
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380

<210> 494<211> 535<212> DNA<213> Homo sapien

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535

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480gacaaaaacc taacttgccg agaaaancaa aatganaatt ggc
523

<210> 496<211> 222<212> DNA<213> Homo sapien

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120cttccacggg ggagacctgg ttgggtgtct cacagaggat gtttccggc tttaggtccc
180tgtggcgat gcctttgtta tgcagaaagt ccaaggcgt gg
222

<210> 497<211> 86<212> DNA<213> Homo sapien

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86

<210> 498<211> 310<212> DNA<213> Homo sapien

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120caggagcccc acccaatgtg caggtggaga cctgcaccag gagtgtcag ggcaagttcc
180ttttcaattg cttccctcgc accaaggga ctgtctatat tctcaccaca taagaacaaa
240aatgtttctg ttcccttac aagtgactac cagtcacca cccatgaagg gctggtccct
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310

<210> 499<211> 403<212> DNA<213> Homo sapien
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403

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240cctatcaggg actatcgcat cgatgagaag aactttgtgg tcgtcatggt gaccaagacc
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334

<210> 501<211> 470<212> DNA<213> Homo sapien
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470

<210> 502<211> 344<212> DNA<213> Homo sapien
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60atgattccaa agtcatctgt aattcttctg tttttgtttt gttctgtott ttcttcattt
120tggttttggg tggggggagg ggcagggtac acaaaggatt tttttttttt ttttttaatt
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344

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240aatgtttctg ttcccttac aagtgactac cagtcacca cccatgaagg gctggtccct
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310

<210> 504<211> 553<212> DNA<213> Homo sapien
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<210> 505<211> 563<212> DNA<213> Homo sapien

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563

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302

<210> 507<211> 227<212> DNA<213> Homo sapien

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227

<210> 508<211> 300<212> DNA<213> Homo sapien

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240tgagacttta tgtggagtga aaattgggca tgccattaca ttgctttttc ttgtttgttt
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<210> 510<211> 397<212> DNA<213> Homo sapien

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397

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120catcgagagc gtgacaggaa atcccaagac tgcttccgcc tcagaggcgt cccggctgcg
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205

<210> 512<211> 496<212> DNA<213> Homo sapien
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496

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630

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120ggttcaaaag ggacctcgg aatcacagg cggggagtcg ccatgtccg gccacagcag
180caggagaaaa tcgggactcc gacctcagcc tccc
214

<210> 515<211> 196<212> DNA<213> Homo sapien
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196

<210> 516<211> 516<212> DNA<213> Homo sapien
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180gctttccctt ttccctgaga ggaagagcac atgttggctt cctcttagtg tgaacgagat
240tgccaggccc ttttctcta tgcacaccan gatagacaan gcaggggata ctggcagcct
300gcattatcct ccattgggnt tacaantgg cctncctttc ttcccttgn nngttgggccc
360caccctngaa aatnngggtt cgccccctcc tntactgccg ggttctccag ggggtgctaa
420atcaaaaaac cccttctgnt ttactanant tgggcagnat ttgacatgnt gataccctt
480gcttnttga tggcacnttc ctggcactct ggggta
516

<210> 517<211> 338<212> DNA<213> Homo sapien

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60gtcaaaaataa cgaaactgcc ccagtaaaaa ggggctgggc ctggggggcca ggaaaggcaa
120gcatgagggc ccagtagagg tggacctgtc cctatggtaa ctgagctcgg cttaaggcc
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240ctagtcactg cctagagcac atggtccccc aocagcctac agcatggaaa caccatgt
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338

<210> 518<211> 378<212> DNA<213> Homo sapien

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60agtgccttga ttgcaggcgt gagccaccga gccagcctc attaatgtgc ttggacctt
120actagtgaaga cccacatttt gccaccatcc acttcatgtt gacaggagcc ctggtctctg
180tcagccttat gtgtttatgc tggagccttt cacttggttc tgagtgattt gccaaagcat
240acagtttcca cgtttggaga ttacctgcc cgggcgggcg ctccaaaggg cgaattcagc
300acactggcgg gcggtactaa nggatccaa ntcggncca aatntggggn aanagnan
360ataantgtt ccgggga
378

<210> 519<211> 319<212> DNA<213> Homo sapien

aaatgttatg acngcactact cccaagaaga accttttctt cagttaagtt aattatacat
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120aaaactccaa ctctattaat ccatgccagt taaacactat aactaaaatt tccaaataag
180cgcaaaagga gatgaagcag ttagttacct ttttgcttga acagtccaaa ggaaaatggg
240tactataaat acagcaggca aactggtaga ctgacctaga acatagtgtt ctaaatttca
300ntntcaaagt ggggctaaa
319

<210> 520<211> 326<212> DNA<213> Homo sapien

cctgacttct gctggcatca agaggtggga gggcctccg accacttcca ggggaacctg
60ccatgccagg aacctgtcct aaggaacctt ccttccctgct tgagtccca gatggctgga
120aggggtccag cctcgttga agaggaacag cactggggag tctttgtgga ttctgaggcc
180ctgcccattg agactctagg gtccagtga tgccacagcc cagcttggcc ctttcttcc
240agatcctggg tactgaaagc cttanggaag ctggcctgan aggggaacgg ctaaggag
300tgtctaagaa caaacnacc cnttca
326

<210> 521<211> 509<212> DNA<213> Homo sapien

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60cctgtatcaa gaacaaaaat gggaggagg gtccacattt atgggtgtgta taggtacat
120ggggaattat ctattctgtg ttttgaaaaa gaagaaatag tgccgtccta ttattttcta
180tatttagaaa ttttttctca agaaatttca attgtatcta tgagatgggt ttctaagat
240cttattgtgt gttataagt ctttttaata tcatactaag tgtgagcttc tggacatttt
300caagagctta cnaaaactaa gtggnatttg gtttttnac cccctggaa nacctanttn
360aaaaggaaa ggcctccaat tttatttggc atgcttcaac cataaagaca ttntgggtt
420cctcgccgc gaccnctaa gggcgaattc canccactgc ggnctacta gtggatccgn
480ctcggnccaa cttgcgtaat catggcata
509

<210> 522<211> 343<212> DNA<213> Homo sapien

cagggtgtct cccagcccc tcctttgact ccaaaccccc gaccacttg ctggggctga
60tccctgtctc atccatgta ccagccactg acaccaaggc acctccaacc cttcaggcag
120agacgactac caaacccaa gccacatctg cccgtcccc cgcctccaa caaagcttcc
180tgtttggaac acagaacacc tcaccttcca gccctgcgc cctgctgca tctcagcat
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300cgcaacacc ctaaggnga aattcaacnc acctggggg cgg
343

<210> 523<211> 369<212> DNA<213> Homo sapien

ccagtctcag gagatgaaca cactcttccg cttctggctc ttcttctcc gagatcact
60caacaaaaag atgtatgagg agttcaagca gctggctctg gaggacgcca aagaaggcta
120cagatatggg ttggagtgc tttttcgata ctacagttat ggcctggaaa agaagttccg
180gctggacata ttcaaggatt ttcaggagga aacggtgaag gactatgaag ctggtaagag

240ccagagttgg atctgagtgga ggacctcggc cgcgaccacg ctaaggggcga attccacaca
300ctggcggggcg ntctaattgga tocanctcgg anccancttg ggggaaaant gggcatantg
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369

<210> 524<211> 353<212> DNA<213> Homo sapien

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60tcattctgga tgatgttctg gatcagcagg gatgcattgg ggtatattat ctctcgacca
120ctgtatgcgg gccctggggt agcttggtga gttcctatta catatcctat aatttgacgg
180ttgccatcca ctctttcacc tttgtaccag ctgtagccaa aaagatgctg gggcagattg
240tggaacaagta gaagcacctc cttccccctc gcgacattga acggcgtgga ttcaataatg
300agccttggcag tggngggcgg ggttcnnaaa ggtanaaatg aagggtgggna ccg
353

<210> 525<211> 272<212> DNA<213> Homo sapien

agccacatgg atgntcacac actcacacct ttgcacacac acacaagctg gctcacagac
60acactggggg cccagatcct ggtcattccc cacagggtctt aataaaggtt catggaagga
120aacctgtttc ctaaggtagg gtgggagtgt gtgtgagtgt gtggggggga gaggggtgaga
180gtgagtgtgn gcgtgtgta ntgtgtgtgt gntgtgnagg agcaggagtgt actgggnnct
240gagtttangg agtnggggaag agganggaga ga
272

<210> 526<211> 653<212> DNA<213> Homo sapien

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60cagagcccaa cttctctgtg gcctatgcc aatgtgccc ctgcctcatg gcgtgaaag
120tgccactac ggaaaagcca acagtgactg tgaacttccg aaagctgttg ttgaatcgat
180gtcagaagga gtttgagaaa gacaaagatg atgatgaggt ttttgagaag aagcaaaaag
240agatggatga agctgctccg cagangaacn angacgcctg aaggaagact ggaanagctt
300tgacatacc ccggggggct nttttggan atttaanttt ttgggaaagt tgttcaacct
360gaanaantta canaggcaat aatcntgact tgtggggcaa actgcttaan aacctgatg
420aanaagtccc ttgagngcct ttgtcgtctg ctcccccca ttggcaaana acctggactt
480tnaaaaaagc caacccccaa tggatcaatt tttcacccnn atggaaaaaa tntttaagaa
540aaaaaactnt tccccttccc tttttcttca ggaantnttg attncaagga caattggggc
600ccccccanggg atangggcca naccttnccc atcntagggg ntgnangaaa aat
653

<210> 527<211> 223<212> DNA<213> Homo sapien

cctcccacga agggcgaaga tggccgagat gatcctaataa ataaccgaag aaagagagga
60ccaaccagaa ttcccttttg acatttgtgt tttttgtttt ttttattttg ttttgtttt
120ctttcttctt cttcttctt aaagacattt aagctaaagg caactcgtac ccaaatttcc
180aagacacaaa catgacctat ccaagcgcat taccaacttg tgg
223

<210> 528<211> 404<212> DNA<213> Homo sapien

cgaggtaaaa cgggtgtgtgt tcggaggggt gaaagcatta agaagcccag tgccctcctg
60gagtgtgaca agggctcggc cttaaggagc tgaagagtct gggtagcttg tttagggtag
120aagaagcctg ttctgtccag cttcagtgc acaagctgct ttagctaaag tcccgcgggt
180tccggcatgg ctaggctgag agcagggatc tacctggctt ctgattctt tggttggaag
240gagcaggaat tcagctccta ttctccaatg gagagatctg gcctcanctt gggctagaga
300tgccaangac ctgcccgcgg gccctntaaa ggggaaattc nancacctng gggccttcct
360tnngatccgn ctcggnccaa cttggcgtaa tatggcatac tgtt
404

<210> 529<211> 357<212> DNA<213> Homo sapien

aaaacttact tcaangnta atttagactc agtaggtaag caacattcag aatatgaata
60tggggaatgac ttgagtttga gtacagatat tcgacaccaa aaaagtcata ctacaatgaa
120ttcctatgaa tgttatcaat gtgggaaagc cttctgccga agttcatccc ttattcgaca
180tcagatcatt cacacaggag agaaacccta taaatgcagt gaatgtggga gattcttcaa
240ccgacgtaca aaccttacta agcatcaaaa acttcatgct gaagcaaagg acctgccccg
300ncggggcgctc caaangnga atttcngccc cctggggggg nggtcnttag ggaagacc
357

<210> 530<211> 179<212> DNA<213> Homo sapien

cgagggtccag attcctcctc tnaagaagcc cctggggagca cagctcatca ccatggactg
60gacctggtgg ttcctctttg tgggtggcagc agctacaggt gtcgagtcac aggtgcagtt
120ggtgcagtcct ggggctgaag tgaagaagcc tgggtcctcg gtgaaggtct cctgcaagg
179

<210> 531<211> 288<212> DNA<213> Homo sapien

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60ctgttaagaa tgtctaatat gcaaagtatt ggaaagcagg catttttacc aaagagcaat
120gtcactataa cttatgaaca gaaagttgtg aaatataagg gtactcatgg aaaccagtga
180agagaggaaa caccggcaat tgttcaacac ggaacagtga gcaggtactt tgggagtaag
240gctctgagag atggaagacg ctgggtctcag atctgaggng atgtctgg
288

<210> 532<211> 320<212> DNA<213> Homo sapien

ccagaagctg aacnttattc acagtgaat cagtaattta gcccggttt gaggtggagg
60ccataatcaa tcctaccaat gctgacattg accttaaaga tgacctagga aacacgctgg
120agaagaaagg tggcaaggag tttgtggaag ctgtcctgga actccggaaa aagaacgggc
180ccttggaagt agctggagct gctgtcagcg caggccatgg cctgcctgcc aagtttgtga
240tccactgtaa tagtccagtt tggggtgcag acaagtgtga agaacttctg gaaaagacag
300tgaaaaactg cntggccttg
320

<210> 533<211> 578<212> DNA<213> Homo sapien

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120ttcggctcag tggaaaacca caaaatgogc cagagggtta tcagaacaga ctgaaagtac
180tctacagcca aaaggccact cctggctcca gccggaagac ctgccgttac attccttccc
240tgccagaccg tatcctggat gcgctgaaa tccgaaatga ctattacctg aacctgtgtg
300attggaagttc tgggaatgtc ttggccgggg actngaanna agtgtncnt ggggagngna
360antttgggac atcctgagct tttgaaatgg acacctgggg aatttatctc tgggctgata
420aaaaggaaact cttgctgggc accacatgtg agtnacttgg atggagacaa acggttcaat
480tangccttcc atggtctact gacantttct gcatgtncct tgactccgag cgtagnnacc
540ccattggcgt ctangtcact ggncaactga antggatg
578

<210> 534<211> 457<212> DNA<213> Homo sapien

taaaattcca aatnntaaat cacttcttgt aggagggttt tcattaactg cagtatatac
60agttcactac atatgggttg tttgagtttt ttgtgtgctg tatttcttct tgttttttaa
120tacctgggttt tgtacataac taactctgtt ctcttttggg tgttcagaaa ctggattttt
180ttttcttaag cagtgcctta tttgtgtttt ttaattttga ttcanaagta tccagctc
240ataggtgttc atactgntac atccaaaaca tttgtcaggc tctctgtcag ctttcatgtc
300atatggnata gaaacatgg aggtaggccn tccnggatnt tttttttaga aaaaaancgg
360tttcccnttg ccgaaccct tagggnaat ccancctgg gggcggtcca ggggaccnac
420tcggaccaac tngcgaanca tggcatactg ttccggg
457

<210> 535<211> 394<212> DNA<213> Homo sapien

cctcagcatc aaagggaaga ctaccatgcc ggggatgaag cgagactgcg ggggtgctgc
60ggcgtcctg ggggccttca gagccgcaat caagcagggt ttcaaagaca acctccacgc
120tgtgttctgc ttggctgaga actcgggtggg gcccaatgcg acaaggccag atgacatcca
180cctgctgtac tcagggaaga cgggtggaat caacaacacg gatgcccgag ggcaggctgg
240tgctggcaga tggcgtgtcc tatgcttgca aagacctggg ggccgacatc attctggaca
300tgacaccttg gcccaacccc ttanggggaa ttccacactt ggggccgtan tagngatcca
360actcggacca acttgggtaa tatggcatac tgtt
394

<210> 536<211> 324<212> DNA<213> Homo sapien

cctaggcaca gaggagcagg ttagggcaca ttcaccttct caggattctg tggctccctc
60attggagaag ggagagagca tcttgggggc gcaattccaa gagcagcgag ggcagaggtt
120agagatggct gagagcccct aacctgaggc ggcaccacaa taggcagcaa caactgtgtg
180gaaagctgga tgaactggtc agtagcggaa aatgggaggg ggcactgggt tggcctcttg

240gggaggggtc caaccttgct tggatgagct catgagaatc ccantgntcc aaacanaggg
 300ggnagaancc aaagccccctt tttt
 324

<210> 537<211> 314<212> DNA<213> Homo sapien

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 314

<210> 538<211> 160<212> DNA<213> Homo sapien

ccaggagccg gngcnaattc atgctgattg ctcagatgga ggaagatgcc cttgtctcga
 60aagctcttac agaaggccat gtccgggtct gtgtcactgc ccgagaacac atccctctgg
 120ggcagctcca tccgcagggt atcaccgccg atcacatagg
 160

<210> 539<211> 401<212> DNA<213> Homo sapien

cgaggctcta tgctgggcaa gggnccttat tttcatatcc agaagttagt cagagcttgg
 60caaataagac ttctctatat aataatgcct ggcccaatgt cccctgtaac atcttacatg
 120caggacgtag ggccaattct ttcataaccc acaggcaact gtgagtgtcc tttctcaaat
 180agtgaaggta ggtattaaag caccctttgtt gggacagatg cacagggttt gcctctgaat
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 300acctgcccng gcggccctcg aaaggngnaa attccacaca cttgngggcg tncnaagggg
 360atccnacctg ggncccanct tggggaatna tggcatactg t
 401

<210> 540<211> 328<212> DNA<213> Homo sapien

ccatggtctt gtgctagaga tggcgggtaca agagtctgtt atgcaagccc gtgtgccagg
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 240ttactaaagg gaggggaaga gccaaagtgg cccgctnact gggccatggg ganaacctnt
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 328

<210> 541<211> 615<212> DNA<213> Homo sapien

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 120acattggga cacattgagc agggctgaaa gaatcaggat tcctgaacct tggatcacac
 180ctccagattt gcaagagaaa atccacattt ttgcccacaa atgtctattc ttgacggaga
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 615

<210> 542<211> 448<212> DNA<213> Homo sapien

tttttttttg ccngggtacc aaatttcttt atttgaagga atgggtacaaa tcaanaaact
 60taagnggatg ttttggttnc acttatanaa aaggtaaagg aaaccccaac atgcatgcac
 120tgccttggtg accaggggaag tcacccacg gctatgggga aattagcccg aggcttagct
 180ttcattatca ctgtctccca ggtgtgtctt gtcaaanaga tattccgcca accagattcg
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 420ccaacttggg gaanttgga tagntgtt
 448

<210> 543<211> 170<212> DNA<213> Homo sapien

aaaaagattt cttgacctat gccttttctt agaaagtttg atagattagt tagaacttca
60gatcatcaga tcagttotcaa atgggtttct tggaatttta tatttgacaa tatttatact
120ataccaaact catttgcagt tcttaggttt gttggttaaa acattttttt
170

<210> 544<211> 572<212> DNA<213> Homo sapien

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420agcaggggga cctgcaaccc cccacccaac cccancaagg gncgtcggna ttcaggacct
480nggncgcgan caccttaggg cgaattccac acacttgccg ncgttactat ggatccaact
540cgnaccaagc ttggggnaat atggcatact tg
572

<210> 545<211> 70<212> DNA<213> Homo sapien

tacaagcttt nttttntttt tttttttttt tttttttttt ttttttttta nttttttnt
60ntttttttat

70

<210> 546<211> 427<212> DNA<213> Homo sapien

cgaggtaaata acctcaaaaa cnggacatca tgacaacttc agtaaagtag attccatgag
60ggtctgatac ctgcagggtt tccgtctgat gacatacttg acctgaaaa atctggggtc
120attttgtttt tcattcttca gcagttaaga tagcggaacg ccgaaaggaa ggagcgtagt
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300ttattaccac tgnctctgct gtacacatgg accttgcccg ggngggcccta agggganant
360ccaacaccct ggngggcggtc ctagnatcc ganctcggac caacttgng aatcatggca
420tactgtt
427

<210> 547<211> 359<212> DNA<213> Homo sapien

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60gtcatctcca cttaaattga tgacacaagc agctaataac catttctggg tttctgccta
120accccctaata tgtctgttaa agccaattct ctgggtgtcc cagtgcgtgg tggctttttt
180tctttccaca ttggcacatt cacttctccc actcttgcca tgtaagaaat aagcatttac
240ataattggaa aaatctggat ttctgatgcc aaagggttaa agcttcttgg atttcatttc
300attgatatac agcccctatt ttatttttgt cagnggcctt tgggcctgt tnaggggcc
359

<210> 548<211> 362<212> DNA<213> Homo sapien

cctccagcca tttngacatt ggggtggata gtgcattcac ctgcctgtca gtgcattcac
60ctgcctgtca ccagttctg tggatgtgtt ggtgctgagc ctttgccttc ttccaaatg
120gttacaggga tgttgatcag ctccaccaga gggagctctg atgggaggaa ttgctctgcc
180atccttgtcc ctgtgtctcc tgtcggcagg cagccattgt atctcaccag cagaccagga
240gactgggtccc aagggttact caccacaggg caatttctg ccatagttag gaaggaaaca
300cctgaactaa aatggnaaaa anaatcctgn gngggtttaa naacacnccc nntgcctttt
360tg
362

<210> 549<211> 318<212> DNA<213> Homo sapien

cgagggtccan gatcntatgc gacaacggcg acaacatcac ccgggtgcag agcgacgtgt
60tcagggtggc ggagttccct cagggctacg gcagctgtga cgagatcccc aggggtggacc
120tcgggtgtg gcaggactgc tgtgaagact gtangaccan ggggcagttc aatgcctttt
180cctatcattt cccaagcaga ctgtctcttn agttcagcta ccaggaggac aagccgacca
240agaaaacaag accacngaaa atcccactnt ttggagacag ggggaacatt tagctacaga
300acctnngtct ttacaca
318

<210> 550<211> 555<212> DNA<213> Homo sapien

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60acaggcaggg cagtaagtac aaagtctaag ctgtaaaaac cgtttgaaaa tataaactcg
120ttttttggaat acatgtgtca aaggctgccc atgttaatac ctttggataa aaacggtaac
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240tacctagtct agtctcaacc acccctgtca gtcaogactc actcctgttc ctttgagggt
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360ggttccaaaa gggccgcncn tgnccccaca agaccgtccc cccagcaca ctatccttaa
420caacatgacn cagaccaacc aaccctaaagt attatctccc nacatctcac ctgtcctgtg
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555

<210> 551<211> 490<212> DNA<213> Homo sapien

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120tgatacaaga gtcagcatca tttaaaggaaa cgtggcagga cttccattctg tgccatactt
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360ccggagnggg ggngaggaca ctggatattt ttagtttttt ttttgtaac anttaaanct
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490

<210> 552<211> 197<212> DNA<213> Homo sapien

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120tataaatcta ggtctcttg gtcattaagg tattaagctt cagtgtcttt ttttttttt
180ttttttttan cccaaaa
197

<210> 553<211> 484<212> DNA<213> Homo sapien

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360atntnaaatg nantgcngag nggaagactt tggncggnaa cccnctangg cgaatncgc
420acactggcg ngctatagt gatcgaattc ggtccaactt ggcgnaatat ggnatagttg
480ttcc
484

<210> 554<211> 200<212> DNA<213> Homo sapien

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60cacatcatag acttcacttc caactccttg gaatgttcat ttctttggct tacaggagag
120actagacagg aaggccaggc aatgcttagg caactaaaat gaggttgggg gtaatgctaa
180cgtcacccctc acagggatgg
200

<210> 555<211> 324<212> DNA<213> Homo sapien

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120gttcccagtt aggtctgggt agggcttctg cacaggttgc taacatattg taagggaagg
180atgcattcaa tataaatata aactcagagc cactggttgt tataaacttc agttcccgaa
240taactctaga agctgtaaaa tcaggagtaa acaatatgat tatatctcta gaagcattgc
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324

<210> 556<211> 349<212> DNA<213> Homo sapien

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349

<210> 557<211> 330<212> DNA<213> Homo sapien
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120cctgaataaa atcaaccaga tacttatgga gaagtacctg aagctgcagg atacctgccg
180tactcagttg gtgtggttgg tacgggaact ggtgaagagt ggggttctgg gagccgatgg
240tgtttgtatg acgtttatga agcagattgc aggtggagat ggtacagnca aaaatattct
300ggnnttgnag aaaaanggtc tggatattct
330

<210> 558<211> 314<212> DNA<213> Homo sapien
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60ctttgtcctc aattaactac ttgaaaatt acagccaagc aaaccacaaa cattttaatg
120gtttatgttt ggatgatatg tctcctgcac atgcttccac cagaacaaaa aaggaaaacc
180aaagaagtgc ctttccacat aaggcacagg acaaaattaa tcccatttac atattcaagg
240cgaaaatgag tgttttctg gcttttgnnt gnttcttttg ctatcacatg tctatagatt
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314

<210> 559<211> 321<212> DNA<213> Homo sapien
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120tgctgcagat tgctctgcca agatacttga aactgtgtt ttattgtggt aattatgttt
180tgtgattcaa acttctgtgt actgggtgat gcaccattg tgatttgga agatagaatt
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321

<210> 560<211> 235<212> DNA<213> Homo sapien
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235

<210> 561<211> 330<212> DNA<213> Homo sapien
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180acatccgcaa agacctgtac gccaacacag tgctgtctgg cggcaccacc atgtaccctg
240gcattgccga caggatgcag aaggagatca ctgccctggn acccacacaa tgaaagatca
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330

<210> 562<211> 348<212> DNA<213> Homo sapien
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120caagcagttt ctttgcgtgg gttactcaag ggcttgtggt tacttgatc tcctctatgt
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240ggaaggcg aggggggtgg gcagtgacta agggacgaaa acatggggaa aatatttcac
300ntttaacatn caaaaaaaaaa gggggggnnt gggggccttc antntggg
348

<210> 563<211> 325<212> DNA<213> Homo sapien
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60cgtggaggac aaggatgctg tggccttttt ntgtgaacct gagactcagg acgcaaccta
120cctgtggtgg gtaaacaatc agagcctccc ggtcagtcac aggctgcagc tgtccaatgg
180caacaggacc ctactctat tcaatgtcac aagaaatgac acagnaantc acaaagtga
240aaccacagaac ccantgagt ccaagcgcaa ngattcaatc atnctgaatg tntctatng
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325

<210> 564<211> 172<212> DNA<213> Homo sapien

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120accacgcac catccagatg aacgtggccg aggttgacaa ggtcacaggc ag
172

<210> 565<211> 203<212> DNA<213> Homo sapien

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120aagccaactg acaaagatgc atcacgtgct ttaggtgatg gccactaccc gatttgttta
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203

<210> 566<211> 510<212> DNA<213> Homo sapien

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60tagttgagat ggcgggcgcc agtgantttt naccagcagg tgaaggcccc ctctgtctt
120ggttggaagc agcggtagct atcgatgaag ggcctacat gagaggcaga ctggcacc
180aagttactga gcaagctgct catccacttg cgccctgggt cctctcaaaa gcattccagg
240ttgactgcat ccantggctc aatggggcgg ggggctgtat tcaagnacc caanaaagaa
300cacatggntg gctgncnccc cggaaggggt tttgttcgga attnccaan aancaanaaa
360agcncntntt aaaaaactan ccgntcagga acttngggcc gnaaaccacc ctaaggggg
420gaaattccan cacactgggg cgggcccgtg actaangaa tccnaactt cggganccaa
480gcttgggcgt aaatcatggg caatagctgg
510

<210> 567<211> 319<212> DNA<213> Homo sapien

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60acagaggagg acagagcaga cagcagatnc catggagtct ccctcgcccc ctccccacag
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240ggtgcttcta cttgtccaca atctgcccc gcacttttt ggctacagct gggccaaagg
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319

<210> 568<211> 340<212> DNA<213> Homo sapien

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340

<210> 569<211> 330<212> DNA<213> Homo sapien

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120ctcaaatgtg tcattggaga tgctgcagtc gatgaccgtc ttcttgctgg tgttgacgat
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330

<210> 570<211> 371<212> DNA<213> Homo sapien

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240aaaaaaaaatc ccaggcctaa ntaatgtcag gcatttttca gacctnggat ttgtaaatct
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360gnataaccaa a
371

<210> 571<211> 342<212> DNA<213> Homo sapien
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60gcccgaggtc cacctactac ttgtctgaca nggacatggt ctgtgctggc cnggggnctg
120atgaggatct gaagaggaca atgatggcct gtggaggctc aatccatacc agtgtgaatg
180ctctgtcagc anattgtctg ggcgatgcc aggtgtttga agagaccan attggaggcg
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342

<210> 572<211> 314<212> DNA<213> Homo sapien
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314

<210> 573<211> 438<212> DNA<213> Homo sapien
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180ttaccacaaa tcctaactgt aagtgtattc atggttattt tcaaaagaat tatgactctt
240cccccacaaa atcctaaaaa acttgaata aacctataaa gctgatttgc atatttacia
300aatttttgaat agcaaataa ggcaactcat atatgtatat aatttttacc tgcccgggcg
360ggcncgcgaa gggcgaaatc tgcagatata catcacactg gcgggcccctc tagcatgntc
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438

<210> 574<211> 253<212> DNA<213> Homo sapien
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120tattatttct ataaatggtn ttgnacattt tttctcaaat aaccacngag tattttattga
180ttgaccannt ctgtgcttgt caacgcattt ggaaaatacn aaaaaaagc tttatgggat
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253

<210> 575<211> 248<212> DNA<213> Homo sapien
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120ccagctgggg gtttaagaatg ttgtttaaga aatgatgacg atatcttgaa aagaaattct
180tggctgggga tggggtaggg ggaacggaa aaacanatat tccttacctc cennccaant
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248

<210> 576<211> 272<212> DNA<213> Homo sapien
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240agaggnngtc ncctttttca ctntactat cg
272

<210> 577<211> 509<212> DNA<213> Homo sapien
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<210> 578<211> 287<212> DNA<213> Homo sapien

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<210> 579<211> 455<212> DNA<213> Homo sapien

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 455

<210> 580<211> 351<212> DNA<213> Homo sapien

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 240cccatctac catctgtggc cccgtgggc cctgacttgc taangcgtg gcgggcatan
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 351

<210> 581<211> 250<212> DNA<213> Homo sapien

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 120aaaaatnttt ctttaaaaaa nnnnggggtt naaaaaaaan tttcncttt ccaaaaaann
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 250

<210> 582<211> 115<212> DNA<213> Homo sapien

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115

<210> 583<211> 294<212> DNA<213> Homo sapien

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 180tctgagtnng tcgncagtaa tcnccact ttactatggt cnccttaacn ttctgaaang
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<210> 584<211> 432<212> DNA<213> Homo sapien

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<210> 585<211> 568<212> DNA<213> Homo sapien

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 540gttantccgg ncggncggcc aaaatggt
 568

<210> 586<211> 345<212> DNA<213> Homo sapien

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 240actcttatgg ggtgtgtgtc tgggcttata anctaactta ttttctcgcg accctagcat
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 345

<210> 587<211> 116<212> DNA<213> Homo sapien

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116

<210> 588<211> 360<212> DNA<213> Homo sapien

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<210> 589<211> 461<212> DNA<213> Homo sapien

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 240ctaagacctg gtgatnttca tnccttcctc tttgctggca aacacctgga ttttctgcgg
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 461

<210> 590<211> 492<212> DNA<213> Homo sapien

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 360acatgtccct gctgtccctg cctaacgcga nggaanaaag aaaaangacc gtgcccagg
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480acacccacct tg
492

<210> 591<211> 377<212> DNA<213> Homo sapien

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240tgtagggaga agcttttagct tcatittact aaaaagattc ctcgttattg ttgttgccaa
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377

<210> 592<211> 401<212> DNA<213> Homo sapien

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120cagctgcagc ggaatcacgc tcaggatgcc tggaggcagt ccacagtgtg gggcagctca
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240ctggcgngcg tgaactntgc agngttctg catttggtgcaa caaggatctt ataataccat
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401

<210> 593<211> 377<212> DNA<213> Homo sapien

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240ctgccaatac ctgatttctg tcccctattt ttccactcgc aatcatatac ttaggtacct
300tttgaccca tgaaaaaaa attctaact tcagaactcc aatacaggaa gaaagaaatt
360ttttttttt tggngng
377

<210> 594<211> 310<212> DNA<213> Homo sapien

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120agaacctacg cactacgtg aggagcttag ccagaaatgg gatggactga acggacagtt
180ccagaagtgt gactggctaa agctcgatgt ggtcacagct gtatagctgc ttccagtga
240gacggagccc tggcatgtca acagcgttcc tagagaagac aggctggaag atagctgtga
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310

<210> 595<211> 434<212> DNA<213> Homo sapien

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434

<210> 596<211> 740<212> DNA<213> Homo sapien

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<210> 597<211> 448<212> DNA<213> Homo sapien

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 120cctcnacatc tctgcttttg gggattttta ccttgtctgc acacttgtca ggggagaggg
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 300acatggtaag cttggcaagg gctncangaa cgcttnacta anggttttan gacccccacc
 360cccatgcctg taccanggct ggctncaga nnagggtgaan aacanaacnn cctgngggcn
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 448

<210> 598<211> 363<212> DNA<213> Homo sapien

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 363

<210> 599<211> 488<212> DNA<213> Homo sapien

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 420tttgaaaana actgtattgg nacnggnagg nggaggangg cttggaangg atnaatatnc
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 488

<210> 600<211> 259<212> DNA<213> Homo sapien

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 120attccacttt ataagaaagg aaactgcttt aattaaagca cgctaataat taaaacttca
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<210> 601<211> 386<212> DNA<213> Homo sapien

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 60gattgccgtg aacctccggc ccggtgacaa gaccaccttc cagctacagg ttccccagggt
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 386

<210> 602<211> 317<212> DNA<213> Homo sapien

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 120gtcagtagcc tgaacagtgg cccaaaggcc actgatcaaa aataaaatag tggctgtata

180tcaatgaaat gaaatccaag aagctttaac cctttggcat cagaaatcca gatttttcaa
240ttatgtaaat gcttatttct tacattgcc aagagtggga gaagtgaatg tgccantgng
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317

<210> 603<211> 378<212> DNA<213> Homo sapien

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60cttcaggcac ctgctgtgcc tccttctcog cagatgctct gggtggaagc ctctgcact
120gccttctgta acagcaccag ctggacgttg tcatgaaatg tcacgagttc tgggtgtttc
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240tctgaggagc tccangacct aggtntctcn cttttgaann gatggnacat gcctngatgt
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378

<210> 604<211> 359<212> DNA<213> Homo sapien

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60aaaaagaaag caaagacagg aagtctactt gccactcag taattaacaa agatttatgt
120aaaattccca caaattgatc tcagaatcag aatcagcatt tntattagc aaaagctggg
180aaatactagt aattgtgctt tatataaagg tgtttgaggc aatctgcata ggaaatatta
240tcaagattca taattgccca gatctgaagg acctgcccgg ggggcnnta aggccgaatt
300cacaccctgc gngcgttntc ttgntccna nctcggacca ctttgcnnat nttgggctt
359

<210> 605<211> 222<212> DNA<213> Homo sapien

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120agtgtggcan caccagggca gccaaagagg gtgnttaaaa ttaacggatc tcttaggggt
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222

<210> 606<211> 507<212> DNA<213> Homo sapien

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60aaaaaacgga aatgtcagaa ttgtatggaa ataaaacttg ttgaaaatt tggaatagt
120ctgctgccag cttatttttc tggacttgtt attttcacat gttaaatgat ctttatatat
180gttgaattaa caaatatttt gagttttcga gaaaaacaa aacatattaa tggattgaa
240atgtgttagt agtctggctg tgtgcccaaa attctgttcg cagcaaaagt gaaagacctg
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360ctaacttggg ngtnngaat gntngcttna tntccgaacn ttttttcct gncggnggc
420cgntcnaang ggncaattcc accccttggg gncggttact attgganccg gntcggtncc
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507

<210> 607<211> 326<212> DNA<213> Homo sapien

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120gcagcgttat acgcagagca atgggcgcag gccgtttggc atctctgcc tcatcgtggg
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326

<210> 608<211> 336<212> DNA<213> Homo sapien

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60gaggctgtgg cactggtgga aaggaggga gaatggagcc tggcccttgt gtgtacaaca
120ggaaatgcac ctgagacac agcaggagtc agcgggaggg cacagacctg cccctgccca
180ggcagaaaat gggcctcctc aagcacaana gtaccaagt acaattttca gttgctaaaa
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336

<210> 609<211> 341<212> DNA<213> Homo sapien

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341

<210> 610<211> 362<212> DNA<213> Homo sapien

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362

<210> 611<211> 76<212> DNA<213> Homo sapien

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76

<210> 612<211> 614<212> DNA<213> Homo sapien

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614

<210> 613<211> 338<212> DNA<213> Homo sapien

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338

<210> 614<211> 243<212> DNA<213> Homo sapien

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120tgtatgtcaa cagaaggat cgtctcttg aagagaactt tactctatcc ttactancc
180catctttcta nggttactcg cgaccctagn atccccgcgg attgacactg cactgcntt
240gat
243

<210> 615<211> 187<212> DNA<213> Homo sapien

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120ggctgtcctt agagcaagcc ctgcctcctg agccaaagga agaaaatgct gaggctgtga
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187

<210> 616<211> 381<212> DNA<213> Homo sapien

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381

<210> 617<211> 315<212> DNA<213> Homo sapien

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315

<210> 618<211> 182<212> DNA<213> Homo sapien

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120gaccaacgat ccatccagat gaacgtggcc gaggttgaca aggtcacagg caggtttaat
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182

<210> 619<211> 133<212> DNA<213> Homo sapien

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133

<210> 620<211> 178<212> DNA<213> Homo sapien

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120ccaccaatgt gggggatgaa ggcgggtttg ctcccaacat cctggagaat aaagaag
178

<210> 621<211> 280<212> DNA<213> Homo sapien

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180ccaccntgt caacagcagg caacctgtgt gttcattttn agtgggatnc agnatttttn
240taaaatgggg cntacntttt ttaagagttt nncacctgaa
280

<210> 622<211> 311<212> DNA<213> Homo sapien

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180cctgaccag ctcttcatgt tcgccggaat gcttaccgtg ctggactgcc gggcggcgctc
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311

<210> 623<211> 269<212> DNA<213> Homo sapien

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60ttatagtaac actctagctg gagtctgggt gacgactggc ancaactccag tactgagaag
120aaaccggata cacagtggca agcaggttgg tgtttatatt tatgacaatg gacatggagt
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240cnaaatagcg cacaaattgg gggaacatg
269

<210> 624<211> 365<212> DNA<213> Homo sapien

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240ctggcgtgga ttctgntaat ggtgatcaca cnttccacct tancctcagc ggagntcttc
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360ctttt
365

<210> 625<211> 391<212> DNA<213> Homo sapien

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180ggagccagac tgcttcaagg acatcgtgaa catgctgatg caccatgaca ggttcaagg
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391

<210> 626<211> 489<212> DNA<213> Homo sapien

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489

<210> 627<211> 442<212> DNA<213> Homo sapien

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240agtgcgtctg aatttgatga tagggcggga gttttgagga gtatcaagct gccaagaagc
300cacttgcaat gacaccagtg agagcatttt ggaagaagaa ccacaagaaa atcaaaagaa
360acttttgct tatnaanaac acctgnggnt tttttgaa ttgtatanaa agaaattgnt
420tnccttctt nccccccca cc
442

<210> 628<211> 316<212> DNA<213> Homo sapien

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120cttcttcagt cgctccaggt cttcacggag cttgttgctc agaccattgg ctaggacctg
180gctgtatttt ccatccttta catccttctg tctgttcaag aaccagtctg ggatcttgta
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316

<210> 629<211> 424<212> DNA<213> Homo sapien

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120cggtgtctt gacattgttg gggatccatt ccacaaagta gctgctgttc ttgttctgca
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240taggatcgnc gtggcggggc cagnagcata tgtcttgatn aaactctggg attcggctg
300ancnacctgt tgttcggtg gaaggnaacc agataaaatg aacnngaagg actgtatgc
360tncgagactt nctgctcgn acccagnatc accatgcgcg tctntgacca ntgtcactgt
420attg
424

<210> 630<211> 339<212> DNA<213> Homo sapien
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120aagaatgagt cagatgagtg tagccatttt aaccaagcag cacatttggt aatttctaca
180acttagtctc agcgataccc attgtattta gccatgttca acaacaagtg tcagaaactg
240cacagactcc tccctgttca gctggtagg agcaattcta ttatttggca ttgcatggct
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339

<210> 631<211> 411<212> DNA<213> Homo sapien
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120acggcatgac cctcacctct atgtaccaga attccaacat ccagatccac cactatccta
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300ttgagatcga ggacaccttt gagacccttc gggtgtgtgt ggtgcatca gggctcaaca
360cgatgcttga aggtaacggc cagtacacgc ttttggcccc gaccaatgag g
411

<210> 632<211> 722<212> DNA<213> Homo sapien
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120ttcttagatt gggaagcaag atgacagttc tgactagctt agttttccag actgaaagta
180atgggaattaa aataatgata actgtagacc ttctccccta aggatgggtc cctggggctt
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722

<210> 633<211> 438<212> DNA<213> Homo sapien
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60tggttgggac agtacagaca gagagaggat ttctgtaact agagaagaac tctataaaat
120gttagcgcat gaggacctaa aaaaagctgg attgctgatt ttgttaata aacaagatgt
180taaagaatgc atgactgtag cagaaatctc ccagtttttg aagctaactt ctattaaaga
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300tgaatggatg atgtcacgac ttaagattag atgatctcta ctgaccctt ctcatagatt
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438

<210> 634<211> 258<212> DNA<213> Homo sapien
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120atccgagaag ttccgaggat tctccttggg ttcttaggg aaccagttgg gatccccaga
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240acaggccatg ttctttcc
258

<210> 635<211> 359<212> DNA<213> Homo sapien
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120aggcaacgct tagcagctgc tgtcctaaca ggctactttc tgcaactgct gacgcaggtt
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359

<210> 636<211> 549<212> DNA<213> Homo sapien

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120tgaggagctg cggggaagta ctccagaggc agcagcccag gtggtgcagt gggtagcctt
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420aggaccttcg ggccgcgaac ccgcttaagg gcgaatttcc acacacttgg gcgggcccgg
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549

<210> 637<211> 645<212> DNA<213> Homo sapien

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60agtcccataa aattaattat tttctctgct tgatcttggg ggacagtttc atgaagctgt
120cagtttagttc attaaagttt tggaaaattc ttcagacagt gcagtgggta tcagaaactt
180gtattcaaga gtacagggtca gactcttctt tttctttctt tttgagatgg agtcttgctc
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480tggttagcttg ttcaaagct ttaaggaga agccaaaca ctggcagnct tccttgaaat
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645

<210> 638<211> 385<212> DNA<213> Homo sapien

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120agttcgagac cagcctgggc aacacagtga gacccccctc tttacaaaaa atacaaaaat
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385

<210> 639<211> 261<212> DNA<213> Homo sapien

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60cctatctgac aagagcatca accctctggg tggctttgtc cactatgggt aagtgaccaa
120tgactttgtc atgctgaaag gctgtgtggt gggaaccaag aagcgggtgc tcaccctccg
180caagtccttg ctggtgcaga cgaagcggcg ggctctggag aagattgacc ttaagttcat
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261

<210> 640<211> 303<212> DNA<213> Homo sapien

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120tgagtggtg ggggtggaga agtaccctgc acctccagt gggcagnagt agacaagggg
180tagcaccaaa cagaaggacc cctcccagc acncacaaca tccaccttca attaccagat
240gcactnctgc tccctaaang aaananacac acanacacac acncacacac acacacacac
300tca
303

<210> 641<211> 295<212> DNA<213> Homo sapien

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120caatcagttt catgaaggag ctcatgcagt ggtacaagga ccagaagaaa ctgcaccgga
180aatgtgccta ccagattctg gtacagggtca aagaggtcct ctccaagctg agcagcgtcg
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295

<210> 642<211> 607<212> DNA<213> Homo sapien

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360actttttgtag ttttgtatgt tactcatctt cttacctgat atcccatgat gatcccatgg
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480aaacaggctt tcttactctg ggttaatttg aagggggttt aatggngatg tcaaaaagtt
540gtntcacanc acttaaatgg gggagccaga cngagaaatg naaagnagtt gattttggac
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607

<210> 643<211> 446<212> DNA<213> Homo sapien

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120tccacggaat aggagattat cccagggtgcc tgtgtccagg ctgggtgtctg ggttctgtgc
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300ggacgcatat gactcaccac gctgtctctg accatgaggc cgccctgagg tgctggggcc
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446

<210> 644<211> 223<212> DNA<213> Homo sapien

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60ccccggtagg gaggtgctga ggtgctgacg tgtctgcact gagtgcacac actgtcgac
120ttgcaactga ccagtggttc ttacagggtg cggagaggcc agcttctcgg tcttcacctc
180caggagggcc gggcttttcc tctccctggt cacgtggagc tgg
223

<210> 645<211> 402<212> DNA<213> Homo sapien

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120cagtactgtt ggttaaatga caatttatgt ggattttgca tgaatacac agtgagacac
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402

<210> 646<211> 109<212> DNA<213> Homo sapien

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109

<210> 647<211> 177<212> DNA<213> Homo sapien

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120gctctgtatg ggaggccatg gccttcgcca gcatctataa gctggacaac cttgtgg
177

<210> 648<211> 240<212> DNA<213> Homo sapien

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120ccacgctgtc aaaaccatcc acgtgctcta agaagagatg cagttccggg tggctggcag
180ggtgcacagt ggcctcgaac agtggcagga agatgttctc cagcatctcc tggaagtcgg
240

<210> 649<211> 501<212> DNA<213> Homo sapien

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120tgctgcgaaa cagaatttttg ggcacacagc cagactacta acacatttcn ataccattaa
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501

<210> 650<211> 325<212> DNA<213> Homo sapien
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180gtgcccctgg tctacaccat aaagcggcac aagtgggtcag tcctgaagag tcggaagctg
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325

<210> 651<211> 223<212> DNA<213> Homo sapien
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120ttgcaactga ccagtgggtc ttacacaggtg cggagangcc agcttctcgg tcttcacctc
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223

<210> 652<211> 476<212> DNA<213> Homo sapien
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420agggggggacc ttgcaacccc canccaaacc cgancaangt tcgtcgcat tcaggy
476

<210> 653<211> 311<212> DNA<213> Homo sapien
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311

<210> 654<211> 412<212> DNA<213> Homo sapien
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412

<210> 655<211> 327<212> DNA<213> Homo sapien
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120agtctgggct gctcccgcac ctgggtgttt atgctgtgta tatatgtgta tccatcctgc
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300aactagtggg tacaaaatgg gagcttt
327

<210> 656<211> 512<212> DNA<213> Homo sapien

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120atccaggaac ggtgtcatgg agccacattc tgcacanact tgatgatgtg gaggggagct
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512

<210> 657<211> 824<212> DNA<213> Homo sapien

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720ngaaaaattt gggaggaana aggggcaatt tttttttt aacttgccg gaacccctta
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824

<210> 658<211> 124<212> DNA<213> Homo sapien

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120tttt
124

<210> 659<211> 135<212> DNA<213> Homo sapien

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120ccatccaaac atttt
135

<210> 660<211> 589<212> DNA<213> Homo sapien

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540ggggaattcc cttggaagtg gntgggcctt tccntgggt tgtttttcc
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<210> 661<211> 251<212> DNA<213> Homo sapien

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120cagggggcagc aggataagga atagagtggg ggcagaaagg tgggttatta aaaaagcatc
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240ccggcgacca c
251

<210> 662<211> 654<212> DNA<213> Homo sapien
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120tgtgtgctgtaa tcaagaggggt cctttggact ggataggag cacttgggag ctgtacacca
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360tcccaagaac cctcgtaatg gcaaaacttc cccaaatgac accccaggac cacagcaatg
420atcttgcgga gaaccagta ggaatcacca tcttaaaaaa tttcaatccc ttttccttc
480cccangggcc gcggtcggtt tccnaagca accnttacct ccaaaaaang gaaaaacttt
540tgaangggcc cccctttggg aacnttggg cccgggaacc nccccctaaa ggggggaaat
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654

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349

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330

<210> 665<211> 171<212> DNA<213> Homo sapien
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171

<210> 666<211> 636<212> DNA<213> Homo sapien
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636

<210> 667<211> 742<212> DNA<213> Homo sapien
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 742

<210> 668<211> 642<212> DNA<213> Homo sapien

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<210> 669<211> 543<212> DNA<213> Homo sapien

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 543

<210> 670<211> 440<212> DNA<213> Homo sapien

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<210> 671<211> 114<212> DNA<213> Homo sapien

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114

<210> 672<211> 177<212> DNA<213> Homo sapien

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 177

<210> 673<211> 439<212> DNA<213> Homo sapien

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439

<210> 674<211> 168<212> DNA<213> Homo sapien
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168

<210> 675<211> 406<212> DNA<213> Homo sapien
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406

<210> 676<211> 222<212> DNA<213> Homo sapien
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222

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530

<210> 678<211> 582<212> DNA<213> Homo sapien
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582

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412

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192

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458

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279

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426

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<210> 687<211> 447<212> DNA<213> Homo sapien

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454

<210> 689<211> 526<212> DNA<213> Homo sapien

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420ggatcttgaa cagcaaaagt ataattgaa aatgcatcac agcatccgga nacacggatt
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<210> 690<211> 468<212> DNA<213> Homo sapien

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360gccaaaagg gtcttaagaa gaaattattt gtttcctcgc gnnccctagc aatccaccct
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<210> 691<211> 102<212> DNA<213> Homo sapien

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102

<210> 692<211> 407<212> DNA<213> Homo sapien

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<210> 693<211> 446<212> DNA<213> Homo sapien

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 446

<210> 694<211> 263<212> DNA<213> Homo sapien

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 263

<210> 695<211> 594<212> DNA<213> Homo sapien

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<210> 696<211> 402<212> DNA<213> Homo sapien

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<210> 697<211> 162<212> DNA<213> Homo sapien

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 162

<210> 698<211> 526<212> DNA<213> Homo sapien

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526

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549

<210> 700<211> 238<212> DNA<213> Homo sapien
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238

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<210> 702<211> 452<212> DNA<213> Homo sapien
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452

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286

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<210> 706<211> 459<212> DNA<213> Homo sapien

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<210> 709<211> 411<212> DNA<213> Homo sapien

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411

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<210> 711<211> 526<212> DNA<213> Homo sapien

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362

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307

<210> 714<211> 503<212> DNA<213> Homo sapien

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433

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341

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378

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176

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339

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559

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571

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168

<210> 728<211> 564<212> DNA<213> Homo sapien

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564

<210> 729<211> 253<212> DNA<213> Homo sapien

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253

<210> 730<211> 291<212> DNA<213> Homo sapien

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291

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<210> 732<211> 203<212> DNA<213> Homo sapien

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203

<210> 733<211> 512<212> DNA<213> Homo sapien

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512

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180

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302

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463

<210> 737<211> 344<212> DNA<213> Homo sapien

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344

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589

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341

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313

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<210> 750<211> 252<212> DNA<213> Homo sapien
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 263

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 240ccctccagcc ctcatatcat gggcttagac gtgttgggat gtttggctgt actctttnaa
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<210> 754<211> 466<212> DNA<213> Homo sapien
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300agccagaaat ctatggtttt gcanaatgga gactctctgc tcangcnaga taaatnccan
360ccaaagcatt agcnttgggn ttctcnccnc cacgtaaagt aacnnctttc ttgggaatcc
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466

<210> 755<211> 469<212> DNA<213> Homo sapien

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469

<210> 756<211> 412<212> DNA<213> Homo sapien

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412

<210> 757<211> 385<212> DNA<213> Homo sapien

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120aagtcctccc ccaccgtccc ccaatgggg gactatgggt tactgtgatc aagagacacc
180tgaacataaa acacaactac acttctacca aaatcaaaact caaatccaca caacaaaaca
240gaattgagca atcttaccag ggattgaaaa ctgagggtgt gagatgctgg gctgagggcc
300angaggagga gaaggaggag agggagggaa agcacaaaat gggaggaggat gagggctcca
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385

<210> 758<211> 290<212> DNA<213> Homo sapien

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120tcttatgaat gttatcaatg tgggaaagcc ttctgccga agttcatccc ttattcgaca
180tcagatcatt cacacaggag agaaacccta taaatgcagt gaatgtggga gattcttcaa
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290

<210> 759<211> 288<212> DNA<213> Homo sapien

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120gtcactataa cttatgaaca gaaagttgtg aaatataagg gtactcatgg aaaccagtga
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288

<210> 760<211> 432<212> DNA<213> Homo sapien

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120gaagaggatc ttacaaagag taagggaaag ggagaggggc agaggctgct tctcagagcc
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240ccactgttgc tggcacgctg gtgcacgtag cactgtggca gatggacctg gagaggaagc
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432

<210> 761<211> 246<212> DNA<213> Homo sapien

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120cggaatgggtg aagcgggaag ggtcttacat gctggttgtc tggggcaagg agactgggga
180agcacagatt ctgcttctca ccccaaacgg tggggttggg ggtgggctga gatgcagacc
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246

<210> 762<211> 411<212> DNA<213> Homo sapien

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300gccgagatgt tcagaaatgg ncccatgtga ccaagttctg ctgtttgggt gacagtgcct
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411

<210> 763<211> 581<212> DNA<213> Homo sapien

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581

<210> 764<211> 253<212> DNA<213> Homo sapien

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120cctgagtcac acgactcacc cagagtcacg gggccagact gggcctgggg tcatggcgcc
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253

<210> 765<211> 270<212> DNA<213> Homo sapien

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270

<210> 766<211> 449<212> DNA<213> Homo sapien

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449

<210> 767<211> 466<212> DNA<213> Homo sapien

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466

<210> 768<211> 459<212> DNA<213> Homo sapien

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360catgaggaag gaacagcaat ggtgtcagta tccaggcttt gtacagagtg cttttctgtt
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459

<210> 769<211> 409<212> DNA<213> Homo sapien

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409

<210> 770<211> 427<212> DNA<213> Homo sapien

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427

<210> 771<211> 524<212> DNA<213> Homo sapien

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524

<210> 772<211> 277<212> DNA<213> Homo sapien

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277

<210> 773<211> 294<212> DNA<213> Homo sapien

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 294

<210> 774<211> 559<212> DNA<213> Homo sapien

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<210> 775<211> 573<212> DNA<213> Homo sapien

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 573

<210> 776<211> 592<212> DNA<213> Homo sapien

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 540ntncccttna anttgntgtc ctttncctt ggtgttntc ccanggatat gg
 592

<210> 777<211> 372<212> DNA<213> Homo sapien

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 372

<210> 778<211> 381<212> DNA<213> Homo sapien

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381

<210> 779<211> 530<212> DNA<213> Homo sapien

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530

<210> 780<211> 465<212> DNA<213> Homo sapien

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465

<210> 781<211> 378<212> DNA<213> Homo sapien

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378

<210> 782<211> 430<212> DNA<213> Homo sapien

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430

<210> 783<211> 364<212> DNA<213> Homo sapien

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364

<210> 784<211> 442<212> DNA<213> Homo sapien

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120ctctgtacca gtgggacaat ctggggggcc taactcagaa gcgaanggaa gctctggagc
180ggaccgagaa actgctggag accattgacc anctgtactt ggagtatncc aagcgggctg

240cacccttnaa caactggatg gagggggcca tngaggacct gcnngacacc ttnattgtgc
300acaccattga ggagatncan ggactgacca cnncccatga ncagttnaag ggcaccctcc
360cttatnccca caaagaacgc ctngactgcc ccggcgggcg cttaanggcg aanttcnaca
420cactngnggg cgntctaata ga
442

<210> 785<211> 359<212> DNA<213> Homo sapien

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120ctcaaggtta ctgggagtggt gggctgccct tgttgccctgc acccttcctt cttccctctc
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240aaactaatct taaccctgtg gtgtcagata ccctgtttct ggagtcacat cantgaggag
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359

<210> 786<211> 367<212> DNA<213> Homo sapien

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120ccattgacca ctgggatcca gtcaacctgg aattgctttt gaaaagnacc cangggcnca
180antggatgga cagcttgctc agtaacttgg ggtgccagtc tgccctnat gtagggncct
240tcatcgatag ntaccgtgc ttccaaccaa accaggaggg ggccttcac cttcttggn
300agcantcact ggncccn cn atctcaacta ntttttccn gcttttnta tngcctggg
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367

<210> 787<211> 476<212> DNA<213> Homo sapien

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360tgnggggtcat ctcaggggtt cttcanctcg gcnacatcgt cttcaaaaag gacggaacc
420tgaccaggcg tccttgcccg ncacncagtt gcccaaaagg ggcccatctc ttnggt
476

<210> 788<211> 538<212> DNA<213> Homo sapien

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120aacacttnog ttacaggaaa tgtatgacgc aaataatata aaattaaaaa gtgaaaaaa
180ggtgacactg gtttcctaag atacaattta ctctttacaa ccagggtcca caggtccagg
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300aatcagccca tgatggcgct atggcctctc agacaccaca cgctgcctaa acacctagag
360ctctggaaat antcaaacag gagaagtgat ttccatgggg gaaaatttta cctgcccg
420gccggcgct cgaaaanggc cgaattncag cccacttggc ggnccgttac ttnttngatn
480ccaggctcng taccaanctt ggcgtgatta atgntcatta cttgnattnt tctgtgtg
538

<210> 789<211> 611<212> DNA<213> Homo sapien

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120taccttacag tatcaacatg aacgtcttcc tcccttgaca tcaactcacct gagaactggg
180cctctacaaa tccagagac cngcgtaac acacatcaag acagaacctg ttgccatttt
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300caccagtata ttcagctcac accagaccgc anctccanag gtggaacaat attttcatca
360aacaagaact tctacaccag atcttcatct ttctntccc taccancaa ggggncacct
420tgtaccagct acttgaatac accgntctct anatatgcc aagttttaca aatcanacaa
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540ttnccccggg ggggncngtt tccaanggn ggaaattcca acacacttgg ggggcgggtc
600tnatngnat c
611

<210> 790<211> 498<212> DNA<213> Homo sapien

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60gagcaccttc tcttctgtgc ttatctcttc aagataaata catggaagga tgcgaaaatc
120ggaacaccaa ctattgtgtc tcacttgcat ctaagtgaag cagccacagc tgtgagagtt
180ttcaaagcag aaagatgctg atgtgacctc tggaaattcag acatactgag ctatgggtca
240gaagtgtttt acttaaaaag caaacaatcc ccaggaaata ctgaatagga accagcaaca
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360acacacatcc ccaaacaata actntcaatc acataggcta attggttcat tattttgnaa
420aaactgacat cctaaccntt ggccctanaa actttcctt ttngnttnaa cntaccctc
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498

<210> 791<211> 333<212> DNA<213> Homo sapien

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120cactgaggag gatgccaaag cttccaagga ggccttgga gacgggaaat tatggaaata
180aagtaccttg gactgggcca aacctaaggg tgaagggtggc ttcgggggtc ntgggtggag
240canaggcggc tttggaggac naggtggtgg tagaggaggc cgaggaggat ntgggtggca
300naggcccggg gagncttgg nagggcgaag gag
333

<210> 792<211> 172<212> DNA<213> Homo sapien

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120tcgagtgta gtcttacgga aacggagccc acctggcatc tctctgagt tt
172

<210> 793<211> 256<212> DNA<213> Homo sapien

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256

<210> 794<211> 310<212> DNA<213> Homo sapien

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120acgatgtcat gaaagatttt gaggagatga ggaagctgggt atctttcaga gtgtaaagta
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310

<210> 795<211> 149<212> DNA<213> Homo sapien

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60ctctctgcct gtttgactt tgtaattatt tttttagcag taattaaaga aaaaagtcct
120ctgtgaggaa tattctctat ttacctgc
149

<210> 796<211> 579<212> DNA<213> Homo sapien

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120aaagatggga gaaataaan cctgttctgg atccccatc ccctccagaa taagagcatg
180ttctgcatgt attaatcttt tatgtgttt atgaaacagg caagataagt ctgtttttcc
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360cattactggg tnatTTTTAA gactatgtac ccacaccata catacctaca tataTNTTAA
420cacatgcnta caaacctgtg tgccnagtga canctatttt tttttatnct tgggtaagtc
480attaaaaatc tgccttngt catcntntta gaattattca aatatttggt gtatatnatin
540aacttnntcc cctcnncccc cttngtnatt nttccctcc
579

<210> 797<211> 338<212> DNA<213> Homo sapien

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120gnnttgcttc ctnttgaggn ttgaaaccac aaccaaaggc tactctnttt tttcttgggc
180nttttggtnt tttnggggtg ttatTTTTgt gggtntttt ttttgnntt aacctttnca
240aacnncnattg gngatnagga atncctttcc anggtctccc aaacacatnt gnggntctgg
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338

<210> 798<211> 140<212> DNA<213> Homo sapien

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60agcttacggg actaggaggc atcttttanga tccaanatg caaantgnca aacctattg
120accngacccg caattatgtt
140

<210> 799<211> 502<212> DNA<213> Homo sapien

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60cccaattgag tgcttcatgc ctttagatgt acaggctgac agagaagatt cccgagagta
120aatcatcttt ccaatccaga ggaacaangc attgtctctc tgccaagatc catctaaact
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420gcgntcgt tacntantgg atcccagntc ggnccnaagg ttngccgtaa tcatggncaa
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502

<210> 800<211> 276<212> DNA<213> Homo sapien

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60catttgatgc acagctgtac aaggaggtgc tagaagcctg cgccctcaat gatgacctca
120gtatcctgcc tgctggagac caaacagagg tgggggagaa ggggtgtcacc cttagcggag
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276

<210> 801<211> 387<212> DNA<213> Homo sapien

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120gttcttctna gattggtttt ttccaccnct ctataaaagt caatcagtct tncagggggn
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240accgtagata caagtacact tcaagcgaca tgctctacaa tattcaagca gtaacnttg
300tgnaccatgn tgggncnagn ntccnagtt gggnggcca caccnnaa aatangncca
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387

<210> 802<211> 542<212> DNA<213> Homo sapien

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540ta
542

<210> 803<211> 542<212> DNA<213> Homo sapien

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 542

<210> 804<211> 452<212> DNA<213> Homo sapien
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 452

<210> 805<211> 141<212> DNA<213> Homo sapien
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 60acaacaccat agccagtata ttagtttgg cttttcctaa catagaaatc ttcaaagctg
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 141

<210> 806<211> 246<212> DNA<213> Homo sapien
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 120gtactgcagc agcgaacatc tcgatatatg aaaactgcat catcaattca acgttttggg
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 246

<210> 807<211> 369<212> DNA<213> Homo sapien
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 369

<210> 808<211> 504<212> DNA<213> Homo sapien
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 504

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 501

<210> 810<211> 554<212> DNA<213> Homo sapien

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 420agataacatc tgctatcana agggttcatt aaattcatgg aacgtgaagg ccgcaggctt
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 554

<210> 811<211> 377<212> DNA<213> Homo sapien

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 60ctctattttt ctcagatatt gtaagcattc tgtttttcaa tattgtagtt aattttttg
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 180ttctgtcann taagggttc actgctttgg tggaaattgg tggaaattgc tagncaggtt
 240ccacgatgnt tatttttttc tccatggttg ggntatcatt acccatttca catacgcggt
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 377

<210> 812<211> 511<212> DNA<213> Homo sapien

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 60cccaattgag tgcttcatgc ctttagatgt acaggctgac agagaagatt cccgagagta
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 511

<210> 813<211> 234<212> DNA<213> Homo sapien

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 120cggcattgatc atttttgcct gatcctttct tttctctctc ttcatctct ttctgcatt
 180cttcaactt tgttttgaat ttctgtgcat tctcagcatt caggaagcgg atgg
 234

<210> 814<211> 258<212> DNA<213> Homo sapien

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 120gccttctgtn acaagcacca agcctggacn gttgnccttg aaattggcac canttcttgg
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 258

<210> 815<211> 145<212> DNA<213> Homo sapien

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 145

<210> 816<211> 231<212> DNA<213> Homo sapien

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120tgacttggtt ttttcagaaa gctaaagtca anaggaatgg gggcntggg ccacntcctt
180tgagantctt taaaatctta cagacaaagc tgtggnaaat gnntaagatg g
231

<210> 817<211> 238<212> DNA<213> Homo sapien

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120ggaactgaga agccacctgc tgttccggcc ctttgggctg tttgggaaaa gccancagtc
180agagtgccag cttcaantnt ctgattatcc ccctnctggg gccctggtag tnnacagg
238

<210> 818<211> 124<212> DNA<213> Homo sapien

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120ctgg
124

<210> 819<211> 451<212> DNA<213> Homo sapien

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120ttgcaattat aaatgttaaa catccctaga gatgaaagtt aaaatgggtg atcacagatc
180agtagcaaaa tacaaattga caattcaaaa ttataaataa aactctgttg aggatgttta
240actttgagtc tccaaattta agagctaagc ttggaagaaa caaatttata gggttatatt
300ccctctttaa ttaaaaaaca aacttcctct ggcagtagtt tgtgaattcc tttcattgta
360atgataccat gattacagga tcaaaaatgc ttaacttact tgccattctg ctcacatcat
420cacagttggt tttttttttt aangcnctca a
451

<210> 820<211> 476<212> DNA<213> Homo sapien

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120tctgtgatca gtgggacaat ctggggggcc taaacttaan aacgaaggga agctctggac
180ggaccgagaa actgctggag accattgacc agctgtactt ggagtatgcc aagcgggctg
240cacccttcaa caactggatg gagggggcca tggaggacct gcaggacacc ttcattgtgc
300acaccattga ggagatccag ggactgacca cagcccatga gcagttcaag gccaccctcc
360cttgatgcc acaaggagcg cctggacctg cccggggcgc ccgttcnaaa gggcnaattc
420caccacactg gnggccgtna ctantggatc ccaactcgga ncaaactttg gcgtaa
476

<210> 821<211> 466<212> DNA<213> Homo sapien

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60gccttttgtt cctccggagg aagaatttat tatgggagtt tccaagtatg gcataaaagt
120atcaacatca gatcaatatg atgttttgac angcatgctc tctactttta taatccggat
180ggtgtgtttac natgacggtc tgggggcngg gaaaaagctt actggctctg aagaccacag
240atgcaagcaa tgangaatac ancctgtggg tttatcaagt gcaacagnct ggaacaagca
300caagccattt gcaaggtttt atccaccgcg ttttgactct gtattaacat ctgagaaacc
360ctgaatcctg caattcaagt agaantcaa cntcatntga aagttcanct gttttcaaaa
420cctgcnatgc ttnaaaatgt tatcccaaan aatncnaaan gcttcc
466

<210> 822<211> 487<212> DNA<213> Homo sapien

aaaaagaaaa aaaaagccaa atacattttc tgacattgta agattgcctt actgtctgtc
60attccttatt gctggccctt ttctcaggcc ggaggccaag tggtaggagaa ggaaaggaaa
120tgatcgaacg ggcattgtgt caaagtgggc atgccactgg gaaataccac cagtttacc
180tgaaacattg tcctcagagg agtaggaaag tggattttga atctctattt tgctcaaaag
240ttcagttcct gagatactga tgactgagag tgctgctggg aaattttcag gattgtgtgg
300tcttttggg ntttttgttt tttttttaa acaaagtga ccgntgttca ctntccacnt
360gatcagttgt aanattacaa tgctgcntgc tanttggtta cataaaanac aanttcancg

420anggaagcgg gttataatng gntggnggg gngtcnaaaa tggncctccn ttttttagna
480nacccca
487

<210> 823<211> 525<212> DNA<213> Homo sapien

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60cataatcaat cctaccaatg ctgacattga ccttaaagat gacctaggaa acacgctgga
120gaagaaagggt ggcaaggagt ttgtggaagc tgtcctggaa ctccggaaaa aagaanggcc
180cttggaagta gctggagctg ctgtcagcgc aggccatggn ctgcctgcca agtttgtgat
240ccactgtaat antccagttt ggggtgcaga caagttgtga anaacttctg gaaaagacag
300ntgaaaaact gcttggcctg gcttgatgat aagaaactga aatccattgc atttccatcc
360atcgncagnc gcaggaaccg gttttncaaa gcnnacagca nctcagctga ttctnaaggg
420ctctccngtt acttctgtgc tacaatgncc tcttccatca aaaccgggnt cctttntnct
480ttttgacacc gagacantan gcattctatg tccnnngaatt gggac
525

<210> 824<211> 317<212> DNA<213> Homo sapien

aaaaataaaa tcaactcaata ggcttaagaa aaatacttta gttcatagtt cattgatctg
60acgtttttgat ttaagatcag gggatgaatc caggatgaaa accaaanana aaaaangana
120aanaangaaa aatatanaag tgantcattt nccatngaaa aanggcattt ccagcctcaa
180cntaaccctca actagttttt attgcattat ttttgaaatg ccaagaaact ggctttggac
240ctgcccgggc ggtcgctcna agggcgcaatt ccncncaactt ggcggccggt actnggtgga
300tccnagctcn gnaccta
317

<210> 825<211> 242<212> DNA<213> Homo sapien

ccatggctag gtttatagat agttgggtgg ttggtgtaaa tgagtgaggc aggagtccga
60ngagggttagt tgtggcaata aaaatgatta aggatactag tataagagat caggttcgtc
120cttttagtgtt gtgtatggnn atcatttgtt ttgagggtag ttgattacn cattgttggg
180ngnggattan ccngttgggt catnagatat ttncangngg ggtcaatac agggggaaat
240ac
242

<210> 826<211> 348<212> DNA<213> Homo sapien

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60tcaccgcgag cactttaatc cccacaacag ccctgtgagg taggaatcac caccattccc
120cccnactcat attacagatg ggggaaaccn agacacacat ttacaaaagc gcgcatacaca
180tggggagttc anggttagcc tgnagtacga acacactttc tccccatggn ccagtcagca
240naccctggc ctnttncccc tcttttana anccccatna tcagcatncn taaaaancta
300acccttnatt ttccccgaan nccctgcat annacagttt ccttccta
348

<210> 827<211> 349<212> DNA<213> Homo sapien

aaaaaaatta taaccttgat tgcttattac aaaaaaattc agtacaaaag ttcaatatat
60tgaaaaatgc ttttcccctc cctcacagca ccgttttata tatagcagag aataatgaag
120agattgctag tctagatggg gcantcttca aattacacca agacgcacag tggnttattt
180accctcccct cctcataaga acttaaaaaa aaagaaaaaa caccctnca aaaaaantca
240aanaatttga ggaaccctt ccaaacagtn cacagttatt aagttcangt ggtcaataat
300tcacatctg cancaaagng tatggacatg atttctttt caaaacttt
349

<210> 828<211> 191<212> DNA<213> Homo sapien

aaacatttgt taagaatcct ttctcatgaa tctctgaata ttggaatgt atttatggag
60tcattaaaat ataattctgg gaagaaacca agaaattaac atttttattc tatatggctt
120tataaatcta ggtcttctgg gtcattaaan gtattaagct tcagtgnctt tttttttttt
180tnngccctaa a
191

<210> 829<211> 447<212> DNA<213> Homo sapien

cctctcattt ttagttaatc acgatttctc tctcttgag atcctctgga ccttctocat
60ctacctggag tccgtggcta tcttccgca gctgtttatg atcagcaaga ctggggaggc
120cgagaccatc accaccact acctgttctt cctggcctct atcgtgcttt gtatcttgct

180aaactggatct ggcgcttcta ctttgagggc ttctttgacc tcattgctgt ggtggccggc
240gtagtccana ccctcctata ctgtgacttc ttctacttgn acattacaaa agtactcaag
300ggaaagaagc tcagtttgcc cngcataagt gccaaanacc atcaccagca tctgtccttc
360aggggtgctcg gacagaattc ttaccacagc aaaagcataa gatgcttgat acngaaaatc
420agaaacttaa ctcttttgtt gcagatg
447

<210> 830<211> 548<212> DNA<213> Homo sapien

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60aacttactct taaaaaggat ggctgccaaag atggaaagtc ttactgggtt ttcattgttaa
120cctattcttt ggacataact atgaattttg tatacaatgc acttcatgaa aagttgtggc
180tccccagat tgcccacaag tgtgatcttg aagtcctaaa catttgtcca tgaagcttc
240aaaaacagcg taactgagtt attcaagtag caagtactta aagatacaat tcttgaagca
300gtttcaatgg tttctgatcc aaataatcag tttctgacat tactacttca cataatagaa
360gccatcttca gtttcttctt cactttctct tttccttttg ggttnccttt ttgtggngctg
420aaggcccan tcttttgggn actatcaana nacttccatt natgnggtnc actggaaaac
480ataanggttg gggattgacn tgcctacctt ggcnnncnt taatctctaa aaaatcaatg
540anaaaaggg
548

<210> 831<211> 183<212> DNA<213> Homo sapien

cctccaggac ctcaagtcaa gggaagaagg aaaaaagaga aaaaagggtga cagaaagaga
60aagatagaac tgggtggttg ggttctgggc agcccatgot tcagccctg caagctgatg
120gtaccgagca tgagactgtg aggtacgggc cccatcacat ggtgctaaca taatctgca
180agg
183

<210> 832<211> 169<212> DNA<213> Homo sapien

aaactgtcgt gtgagaaact tttatattag gccatttga ttttattaag tgctaaggaa
60agaggggctta caaatgttt cgtaaatatt ttatactgtt taagtgttaa acaccaaccc
120tgtctttctt ttgggttgag cttttttaga aagtcgaagt gaatgttg
169

<210> 833<211> 351<212> DNA<213> Homo sapien

ccatgttggt gggcanctgt ccacccatgg ataggatcac accttcaggg ttctcgagct
60catagatgtc catcaccacc tcaaaagaga tctcatcaaa gtagagtga tcacacatgt
120catagtcggt gctgactgtc tctgggttat agttcaccat gatggtctta tatcccatct
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240ggtagacgcc agagccaagg actaggacat gaggtgttcg aaaggtagg tcatgggtg
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351

<210> 834<211> 478<212> DNA<213> Homo sapien

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120cagttaccaaa agcctagata cgcgttagat ggccttttcc cgttctgtgc gtttgcctg
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240aacggcacaac gcagcagcta aagcaccgca ctttgcctg ctaacctttt cttaaatgag
300gttttgccaa atccacatct ggaaccgcgt ccaccattt tgcaaggatg tttgtncctt
360gatgaaactg catctctact gcacatgang gcttttnatt tgtanggaca agaanganga
420ngttccgntt atttttgtaa cntgntttac attggttccg atntaagtna aattcggg
478

<210> 835<211> 421<212> DNA<213> Homo sapien

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60cctggtcttg gaagggaaga gaaaaagac gcaggccacc tgggggttct gcagtctttg
120gtcagtccag ctttctatct tagctgnctt tggcttccgc agtgtaaacc ttgcctgcc
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240tcaagcttgc ctttcccttg agtccctctc tcccctcngn tctagccaga ggtgtagcct
300gcagatctat gaaganaaga actgggggag gaggatgaag gacctcgcc gcgaccacc
360taagggcgaa attcancaca ctgncggccg tnactagnng ntcctagctn gnaccaatct
420t

421

<210> 836<211> 515<212> DNA<213> Homo sapien

tgaacacaga ggactcacca tggagtttgg gctgagctgg gttttcctcg ttgctctttt
60aagagggtgc cagtgtcagg tgcagctggt ggagtcctgg ggaggcgtgg tccacctggg
120aggtccctga aactctcctg tgcagcctct ggattcacct tcagtagtta tgctatgcac
180tgggtccgcc aggtctccagg caaggggcta gagtgggtgg canttatagt atttgatgga
240aataataaat actatgcaga ctccgtgaag ggccgattca ccatctccag agacaattnc
300aanaacacgc ttgtctctgc aaatgaacag cctganaagc tgaggacacc ggctgtgtat
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420aggggnacaaa ttngggtcna ccctnttttt tttccngccc tccccacccc aaagggggng
480cncccattcc gagtgtcttt ttncnccct atggg
515

<210> 837<211> 416<212> DNA<213> Homo sapien

gnngacacac tcaccctgga ggagaggggc cacttcaaac agcggatcac cgcagacctg
60ctgtccaacn gcctcggtg gtacccccc aaggaatttg atgaggactc ngaggaccgg
120ctggtgaacg anaagttccc ggacatgac catttcttgt ggtgggcagt gaccaccatt
180accaggtcaa cggtaanaag gattcttttg aggaagacca aaggggggn accatccaan
240ttgaaaaaca ccncnactg tcgagtttgc ctactgcgg gacctntca tnangacngc
300acatncnaaa cattcaaang acattaccna ctantcttc acttttaang cctaccctnn
360ttgnaaacn ccttaactat gggcntngtn ttcctttgna coctngtncc ttatcc
416

<210> 838<211> 58<212> DNA<213> Homo sapien

ctgantcaag ccaaaaaaaaa aaaaacccaa ancaannaa aaaancantt aagncctt

58

<210> 839<211> 193<212> DNA<213> Homo sapien

gggtggtttg cttaggcgca gacggggaag cggagccaac atgccagtgg cccggagctg
60ggtttgtgc aaaacttatg tgaccccgcg gagacccttc gagaaatctc gtctcgacca
120aaaanttgaa ncttgatcgg tgagtatggg ctccggaaca aacgtgaggt ctggagggtc
180aaatttacc tg
193

<210> 840<211> 468<212> DNA<213> Homo sapien

cctcgaaagt gctccgcgta aactacacgt tgaaagtga cgtgttattg gcatttcatt
60caaattccatg aggagaaaaa actacgggag gaaatcttac aacaccattg ctgccaccac
120ctgcaagggn cagctttctc actaggatgg aaaagaagcg tttctgagga acaattcaca
180ttagtacaaa aaaatgatac agccatttcc aaagagcaga gtaatgatca caatggcagt
240ttcgaggaat ccagggtcag tctcacacg ggcctcacc agcctctccc gagtggcgac
300ngcgtgaga gccanaaagg gggcaacgag aagacnagtt tntagcgacc cttgggaaaa
360gcctacgcta cacatttcag aggagattaa aacattccat atgccattta actttaacct
420aaaaaaaaata tagtgggagg gaacctttgn nttcnagaa attcaaag
468

<210> 841<211> 449<212> DNA<213> Homo sapien

ccatcagcag accaggccag ggaggtgcac tggggtggtt ctgccttgc gctggtactg
60ataacttctt gcttcagttc atctacaatg atctttccct ctaaattcca gatcttgatg
120ctggggcctt gtggnacnac acagccagta gcggttaggg ctgaagcaca gggcggtgat
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300canttgagg acttgagac agcttctatg agtatttgc gaaggacctc gggcgcgacc
360accctaagg cgaattccan nacactgcgn gccgttacta attggatccc aancctggtc
420caacctttgc gnaatcatng gtcatttct
449

<210> 842<211> 177<212> DNA<213> Homo sapien

ccaacgggg catccactac atcaccttgc atggcgtgt ctacgacctg catggctcct
60gtcctatgt cttggcccaa gtctgccacc caaagcctgg ggacgaggac ttttccatg
120ngcttgaaaa aaaatgcagc ttggagatct ccaacgcctc ctggttactg tggctgg
177

<210> 843<211> 123<212> DNA<213> Homo sapien

cctccacgct gagtacacct gaggaaccct gggagctcag gaaggaagga gcacccanaa
60gcagggacan ggagctggtt ggggaggacc anaaatcagg ttatcaatac ttttgntga
120cca
123

<210> 844<211> 507<212> DNA<213> Homo sapien

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120ganacaaaa acccttgat tttcgtgca cgggacacgg tcaactgtc ttcctcagaa
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360acantacatt ggttgcatc caaatgggca aaccgttnta ncanggggca ggggtcangt
420caagttatcn agcnggcaca tagatagcnc tgtacagang ggatanatcc cttttgtna
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507

<210> 845<211> 434<212> DNA<213> Homo sapien

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60attactccgg tctgaactca gatcacgtag gactttaatc gttgaacaaa cgaaccttta
120atagcggctg caccatcggg atgtcctgat ccaacatcna ggtcgtaaac cctattgttg
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240gttattggat caattgagta tagtagtncg ctttgactgg tgaagtctta gcattgtact
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360annttttagg acctgtgggg tttngtaggn acntggctcg catnntatac gattaananc
420tccantnggg gctt
434

<210> 846<211> 317<212> DNA<213> Homo sapien

ccaggcgtct gcgaaatcat atggctgtag cattcgtgct atccctgggg gttgcagctt
60tgtataagtt tcgtgtggct gatcaaagaa agaaggcata cncagatttc tacagaaact
120acnatgtcnt tgaaagattt tgaggagatg aaggaaggct ggtatcttcc anagtgtaaa
180gtaatcttgg aatataaana atttcttcag gntgaattac ctanaagttt tgctactgac
240tcgtgttctt gaactatgac acatgaatat gtgggctaag aatanttcc tcttgataaa
300taaacattt acaaaact
317

<210> 847<211> 464<212> DNA<213> Homo sapien

aaaaaccact tgactagcga ctgtactgtt tcctcgtggt tcaggggtgt gcatgaaggc
60tcttangaga gcaaacacct gttcctactc tgtatgtccc tccctcattt caaatgagaa
120gtaaccaatt tngtaaaaa taaccaata accattgcc caccatgaac atggggcttg
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300nttgtaggg tgtctgantg tctatgtgag ggcaaggaca acantgcagt ccaataaaca
360canaaaaaat tgctttttt gcanctgaag ctctgtnttg ganatttcat tttgttact
420gggacagngc ttaattcatt cccaaagtcc tttgnaaca cctg
464

<210> 848<211> 561<212> DNA<213> Homo sapien

aaaggagatt cccaggagct gctacatgac acttactgtt gactagagtt tagtcacaaa
60atttatttgc gaaggagtct gtgaactgta gtctttatc ttgggtcaa aatcagaggc
120tgtattacaa aggaagaaaa gagtgtatc aggggagcaa ctacttctc gtgcacagaa
180tccaagggca gagggtgtc tgaaagggg gatgtgtcag tatcacaaa acaatcaaga
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480tggaatgag ggattaaagg gctntanaaa accaaaagga ctgctgttaa aggacaggt
540tgannangaa ggagaccccc t
561

<210> 849<211> 428<212> DNA<213> Homo sapien

ccttggcata tgccccaatc aacagctgct gttttcctgg aatagtcctt gagtaatccc
60gcaggtactt ggagagttcc atctcaatgg ccccgccacc agccaccact gaatcattct
120tgatgggnccc tcctgacnat catgatggca tcatgcaggg accgctctgt ctctccata
180aactgctcgg cgccgccacg gagaatgaag gtgcatgtct tggccttggg gcagccagta
240aaaaaattgt acctctcgcc tccaatctgg gtctcttcaa acacctggca tgcaccagc
300acatctgctg acagagcatt cacactggtc tggattgagc ctccacaggc catcattgtc
360ctcttcagat cctcctcagg tactcgcca gcacagaaca tgttcctgtc agcaaagtac
420tgggtggg
428

<210> 850<211> 391<212> DNA<213> Homo sapien

aaatactggg ggccattaag agtggatgta gctaagagct tagctaacat tgccttttca
60ctctattttt ctgagatatt gtaagcattc tgtttttcaa tattgtagtt aattttttgg
120ctttcaacaa gcagccctag taatgggtga gttgttaatt aatgtgtata ttgtactgaa
180tttctgtcag ttaaggggtt cactgctttg gtggaaattg gtggaaattg ctgacaggtt
240ccacgatgtt tatttttttc tccatgttgt atatcattac catttcacat acgcgtttct
300atttttcttc ctctcctcct gatctcctta aaaatgaatc tagagttggg ggctttttcc
360ccctcctctt tggacctcgg ccgcgacca c
391

<210> 851<211> 329<212> DNA<213> Homo sapien

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60tncaaagcct gaacgaccgc ctggcctctt acctggacag agtgangagc ctggagacct
120agaaccagan gcttgggaana gcaaatccg ggagcacttg nanaagaagg gacccaggt
180caganactgg agccattact tnaagatcat cgangacctg agggctcaga tcttngcaaa
240tactgtggac aatgcccgna tngttctgca gattgacaat gcccgntttg ctntctgatga
300ctttanagtn aagtntgaga cagagctgg
329

<210> 852<211> 279<212> DNA<213> Homo sapien

ccttccttgc caggacctag agtttgttca gttccacct acaggcacat atggtgctgg
60ttgtctcatt acggaaggat gtcgtggaga gggaggcatt ctcatthaaca gtcaaggcga
120aaaggnntaat ggagcgaata cgcccatcg cgaaggacct ggcgtctaga gatgtggtgt
180ctcggtggat gactctggag atccgcgaag gaagaggctg tggccctgag aaagatcacg
240tctacctgca gctgcaccac ctacctccag agcagctgg
279

<210> 853<211> 267<212> DNA<213> Homo sapien

catggctagg tttatagata gttgggtggg tgggtgtaaag gagtgaggca ggagtccgag
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267

<210> 854<211> 335<212> DNA<213> Homo sapien

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<210> 855<211> 348<212> DNA<213> Homo sapien

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240acaaagagac agaaggatga aaaagaagaa gagggagggtg gtggggacgg cgtcatcccg
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348

<210> 856<211> 371<212> DNA<213> Homo sapien

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371

<210> 857<211> 358<212> DNA<213> Homo sapien

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358

<210> 858<211> 346<212> DNA<213> Homo sapien

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180gggaaggctg tggtgctgat gggcaagaac accatgatgc gcaaggccat ncgagggcac
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346

<210> 859<211> 380<212> DNA<213> Homo sapien

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380

<210> 860<211> 328<212> DNA<213> Homo sapien

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328

<210> 861<211> 346<212> DNA<213> Homo sapien

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346

<210> 862<211> 209<212> DNA<213> Homo sapien

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209

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328

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563

<210> 865<211> 538<212> DNA<213> Homo sapien
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538

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534

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295

<210> 868<211> 461<212> DNA<213> Homo sapien
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 327

<210> 873<211> 446<212> DNA<213> Homo sapien
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302

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374

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329

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538

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278

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231

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445

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414

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554

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108

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301

<210> 885<211> 136<212> DNA<213> Homo sapien

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136

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399

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326

<210> 888<211> 531<212> DNA<213> Homo sapien

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120tgccattaag ggtgtgggcc cgaagatatg ctcatgttgg tgttgaggaa agcagacatt
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 240atgcagaatc cacgccagta caagatccca gactggttct tgaacagaca gaaggatgta
 300aaggatggaa aatacagnca ggttctancc aatggtctgg acaacaanct tcgtgaagac
 360cnggagccga ctgaagaana ntcnggccca tagagggtcg cgttactttt tggggccttc
 420ntgnccgagg gccancnaca nccaaaanct cttgngcgcc cgcnggccgc acccggtggg
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 531

<210> 889<211> 581<212> DNA<213> Homo sapien
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 180tgatcaatgc aggagtcctg tacctctact tcagcaatta cctacagatt gatgaggaag
 240aatatggtgg cactgtggag ctacgaagg aagggtttat gacctctttt gccttggtca
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 420ggggaacccc anccccttgg aacttgaag acnctgttt tctgnacccc gaatcaacng
 480tggtgggcat canngttttc tgcaangggg tngancctga aaacttttac ctgcccgggc
 540ngcccgcctc nagggggaat tcncnacnct tggcggtctt t
 581

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 60gtcactaata gaatgtctcc aaagctggat tgatgtggag aaaacacctt tcccttctag
 120ttttgagaga ctctctcttg gctcccagga ggagggttc cctgactttg acacacatgg
 180

<210> 891<211> 124<212> DNA<213> Homo sapien
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 124

<210> 892<211> 87<212> DNA<213> Homo sapien
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87

<210> 893<211> 420<212> DNA<213> Homo sapien
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 120agaacgtccg atttggagat agcgggagga caggaaggag tggggccat tttggtctg
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 240cttgacgac acacagcgtc ccttgatgct cgatngggac cccaaacggg ccttgganac
 300ctaaccacccc ccnccnnaa gggngttnag ggttttttct ttaangntt aaaangaat
 360nctttttntg ggnnttcctt ggntaacngt taaaaanaa aaanngggg gaaaagggtt
 420

<210> 894<211> 314<212> DNA<213> Homo sapien
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 120cacagggtct tagattggga agcaagatga cagtcttgac tagcttagtt ttccagactg
 180aaagtaatgg aattaaaata atgataactg tagaccttct tccctaanga tggtgccctg
 240gggnttttgg gaaaccagg atggaggag aatactgctn actnttcan cttaggggct
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 314

<210> 895<211> 353<212> DNA<213> Homo sapien
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 120gtctgaaga gaggaagaaa aacttttttag aggaacttaa tggtaacata aaccaaactc
 180ccactgtatt agtatttgag acaagattac atctatgcat tcacacagct tgtctgtaga

240tctgagagct ccaagggagt ggcccagccc ccattcctct gactttagcc ttctgaaaaag
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353

<210> 896<211> 435<212> DNA<213> Homo sapien

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300aaaattgagn tcgnttgngg ggttttacaat tccccnccgn agggnaaaat ngggggtaan
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420tgagtggngc cccac
435

<210> 897<211> 331<212> DNA<213> Homo sapien

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180aacgagccat cttctgggt gctcagaagg aggcagattt ggctgcccga gaagaagctg
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331

<210> 898<211> 690<212> DNA<213> Homo sapien

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120cagggaggaa ttgaagtag atagaaaccg acctggatta ctccggtctg aactcagatc
180acgtaggact ttaatcggtg aacaaacgaa cctttaatag cccctcccc tccggatgtc
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360gttcgctttg actgtgaag tcttagcatg tactgctcgg aagggtgggt ctgggtccnaa
420ggnggcccc aacnaaattt taattccggn ttgggaantt nggacctggg ggttggttagg
480actgttgnt aataaattaa actccatagg tntctgctgn tnggtatgcc cncctttcgg
540gcaggcaatt tactgttaaa gtanaaanag tgacctctga accttatcag ccnatttagg
600acanggatat gttcctcccc cgncgccc ncnctgtnact tttatngngg gggnttttac
660ngngagtaga gggagnttg taannggggt
690

<210> 899<211> 432<212> DNA<213> Homo sapien

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120ttgactttat ggagaatatt tcaactggaag gaaagactaa cttctttgag aagagagtag
180gcgagtatca gaggatggga gtgatgtcaa gtccaacaga gaattctttt acctgggatg
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300taanaaaaaat caagtgaag ggtccacct tcccccccc ngaaatggcc cgnaggtttt
360taacaaantt ttttcttccg gggggccctc aaangngaa ttccncccn gggggcngtc
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432

<210> 900<211> 378<212> DNA<213> Homo sapien

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180aacagagtcg tggaggcttt gaactcttca gaaaaaagga aagacaggaa agctcagaaa
240caaagagaca gaaggatgaa aaagaagaag aaggaggtgg tggggaccgc gttattccct
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378

<210> 901<211> 438<212> DNA<213> Homo sapien

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 438

<210> 902<211> 327<212> DNA<213> Homo sapien

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 327

<210> 903<211> 262<212> DNA<213> Homo sapien

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 180ctgctcaaac acacacattc ttttctggtt gcccnnattg taaattattt nangagctgg
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<210> 904<211> 482<212> DNA<213> Homo sapien

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 180aacaagtcg tggaggcttt gaatctctca gaaaaaagga aagacaggaa agctcagaaa
 240caaagagaca gaaggatgaa aaagaanaa aaggaagtgg tggggaccgc gtcacccctt
 300gaaganctta antnttggat taattggtgg gnttgggggn naaccctccc cccaggggng
 360gactgcccgg cggccttnaa ggggaattca nncncttgcg gcgttattnn ggatccaact
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 482

<210> 905<211> 224<212> DNA<213> Homo sapien

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 120ccagctccag cagccttctt gtccactgct ttgatgacac ccaccgcaac tgtctgtctc
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 224

<210> 906<211> 326<212> DNA<213> Homo sapien

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 326

<210> 907<211> 369<212> DNA<213> Homo sapien

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369

<210> 908<211> 211<212> DNA<213> Homo sapien
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211

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331

<210> 910<211> 325<212> DNA<213> Homo sapien
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240agactttgaa gaaacttttg gatgtggggc atcatccgca tctttctctn tcctccaaat
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325

<210> 911<211> 313<212> DNA<213> Homo sapien
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313

<210> 912<211> 360<212> DNA<213> Homo sapien
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360

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415

<210> 914<211> 314<212> DNA<213> Homo sapien
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314

<210> 915<211> 403<212> DNA<213> Homo sapien

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403

<210> 916<211> 83<212> DNA<213> Homo sapien

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83

<210> 917<211> 347<212> DNA<213> Homo sapien

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347

<210> 918<211> 339<212> DNA<213> Homo sapien

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339

<210> 919<211> 102<212> DNA<213> Homo sapien

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102

<210> 920<211> 504<212> DNA<213> Homo sapien

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504

<210> 921<211> 447<212> DNA<213> Homo sapien

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120tccacagtcc aattccactt caattgatag acccaaaaaa tataatttaa tcaaagttct
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447

<210> 922<211> 375<212> DNA<213> Homo sapien

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120tcctgggcat ggagtcctgt ggcattccacg aaactacctt caactccatc atgaagtgtg
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240acctggcat tgccgacagg atgcanaagg agatcactgn cctgggnacc agcacaatga
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375

<210> 923<211> 479<212> DNA<213> Homo sapien

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348

<210> 927<211> 319<212> DNA<213> Homo sapien

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319

<210> 928<211> 335<212> DNA<213> Homo sapien

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<210> 929<211> 411<212> DNA<213> Homo sapien
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<210> 930<211> 349<212> DNA<213> Homo sapien
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<210> 931<211> 220<212> DNA<213> Homo sapien
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<210> 932<211> 307<212> DNA<213> Homo sapien
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<210> 935<211> 196<212> DNA<213> Homo sapien

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<210> 936<211> 384<212> DNA<213> Homo sapien

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390

<210> 938<211> 300<212> DNA<213> Homo sapien

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300

<210> 939<211> 301<212> DNA<213> Homo sapien

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301

<210> 940<211> 472<212> DNA<213> Homo sapien

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 306

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341

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370

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654

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283

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360atgagggagc acagagccac ttgcagagag gattgcctgg gagggggaag gggaagaatc
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692

<210> 957<211> 327<212> DNA<213> Homo sapien

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180gagactggag ccattacttc aagatcatcg aggacctgag ggctcagatc ttcgcaaata
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327

<210> 958<211> 220<212> DNA<213> Homo sapien

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220

<210> 959<211> 462<212> DNA<213> Homo sapien

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360aatctgggga aacaagacat ttacctgccc gggcggnctcg ctcgaaaggg cgaattncca
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462

<210> 960<211> 396<212> DNA<213> Homo sapien

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396

<210> 961<211> 582<212> DNA<213> Homo sapien

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582

<210> 962<211> 114<212> DNA<213> Homo sapien

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114

<210> 963<211> 601<212> DNA<213> Homo sapien

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600a
601

<210> 964<211> 560<212> DNA<213> Homo sapien

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560

<210> 965<211> 223<212> DNA<213> Homo sapien

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120ttgcaactga ccagtgggtc ttacacagtg cggagaggcc agcttctcgg tcttcacctc

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223

<210> 966<211> 425<212> DNA<213> Homo sapien
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425

<210> 967<211> 339<212> DNA<213> Homo sapien
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339

<210> 968<211> 291<212> DNA<213> Homo sapien
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291

<210> 969<211> 130<212> DNA<213> Homo sapien
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130

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210

<210> 971<211> 122<212> DNA<213> Homo sapien
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120tt
122

<210> 972<211> 108<212> DNA<213> Homo sapien
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108

<210> 973<211> 313<212> DNA<213> Homo sapien
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313

<210> 974<211> 272<212> DNA<213> Homo sapien

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180tactagcata ggttcagcac caagcnaat gttatittac tggtingcct ttttcattct
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272

<210> 975<211> 375<212> DNA<213> Homo sapien

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375

<210> 976<211> 340<212> DNA<213> Homo sapien

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340

<210> 977<211> 429<212> DNA<213> Homo sapien

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429

<210> 978<211> 390<212> DNA<213> Homo sapien

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390

<210> 979<211> 372<212> DNA<213> Homo sapien

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372

<210> 980<211> 261<212> DNA<213> Homo sapien

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261

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266

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199

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344

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400

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232

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347

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256

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380

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366

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302

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569

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362

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374

<210> 996<211> 304<212> DNA<213> Homo sapien
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304

<210> 997<211> 344<212> DNA<213> Homo sapien
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344

<210> 998<211> 542<212> DNA<213> Homo sapien
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540cc
542

<210> 999<211> 285<212> DNA<213> Homo sapien
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285

<210> 1000<211> 133<212> DNA<213> Homo sapien

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133

<210> 1001<211> 112<212> DNA<213> Homo sapien

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112

<210> 1002<211> 273<212> DNA<213> Homo sapien

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120atggtggttaa ctgataatag cactaatgct ttaagatttg gtcacactct cacctagggtg
180agcgcatgga gccagtgggtg ctaaatgcta catactccaa ctgaaatgtt aaggaagaag
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273

<210> 1003<211> 585<212> DNA<213> Homo sapien

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585

<210> 1004<211> 576<212> DNA<213> Homo sapien

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576

<210> 1005<211> 436<212> DNA<213> Homo sapien

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436

<210> 1006<211> 438<212> DNA<213> Homo sapien

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438

<210> 1007<211> 116<212> DNA<213> Homo sapien
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<210> 1008<211> 220<212> DNA<213> Homo sapien
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120gctttctctag tggagatggc tatttcgaaa acagcccact gatgtcccag ccagtgtggg
180agaggcatcg ccctgataga ttctgaatt ccaactcagg
220

<210> 1009<211> 96<212> DNA<213> Homo sapien
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60ataccaaggc caccacacac cactgtcca aaaagg 96

<210> 1010<211> 550<212> DNA<213> Homo sapien
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360gcacaaagat gtcttgatca aggaaggaa atcnacctn aaagttnaat ggcgaanatt
420gcatttgcac tgtnggtccc tnaangaaaa gagaaaaaaa gtnccactnt tccagannat
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550

<210> 1011<211> 334<212> DNA<213> Homo sapien
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334

<210> 1012<211> 50<212> DNA<213> Homo sapien
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<210> 1013<211> 434<212> DNA<213> Homo sapien
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434

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120taccttacag tatcaacatg aacgtcttcc tccctgacat cactcacctg agaactggcc
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552

<210> 1015<211> 344<212> DNA<213> Homo sapien

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120ctcaacgaag gcaaacacct ttacacgcta gatggtgggg acatcatcaa cgcctgtgc
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344

<210> 1016<211> 304<212> DNA<213> Homo sapien

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120tactttgccc tgcccacatt gcaggtgttt tgtatatata caatggataa attttaagt
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304

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120ttttcctttg gagaactcaa atgcttccgc aacattatc ttattcttac acaatttag
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250

<210> 1018<211> 375<212> DNA<213> Homo sapien

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375

<210> 1019<211> 280<212> DNA<213> Homo sapien

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280

<210> 1020<211> 365<212> DNA<213> Homo sapien

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360ggtg
365

<210> 1021<211> 425<212> DNA<213> Homo sapien

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425

<210> 1022<211> 131<212> DNA<213> Homo sapien
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60cctaagaaca agtgggcgat ggnngcatat gcatnntcct ttctggggat tcaaaaacag
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131

<210> 1023<211> 213<212> DNA<213> Homo sapien
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213

<210> 1024<211> 303<212> DNA<213> Homo sapien
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303

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356

<210> 1027<211> 425<212> DNA<213> Homo sapien
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425

<210> 1028<211> 577<212> DNA<213> Homo sapien

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480ttgaagccaa gctttcactt cttaaagtgc ctaccgagac tttgtaaatg naaaatgcag
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577

<210> 1029<211> 331<212> DNA<213> Homo sapien

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220

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243

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156

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398

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<210> 1067<211> 515<212> DNA<213> Homo sapien

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 420gaactacatg gtccanctgg ggaagctgct gggcggcggg ggacnaggaa gccatccggc
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<210> 1068<211> 353<212> DNA<213> Homo sapien

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<210> 1070<211> 108<212> DNA<213> Homo sapien

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108

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<210> 1072<211> 377<212> DNA<213> Homo sapien

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 433

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<210> 1079<211> 246<212> DNA<213> Homo sapien

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246

<210> 1080<211> 220<212> DNA<213> Homo sapien

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<210> 1081<211> 253<212> DNA<213> Homo sapien

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253

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223

<210> 1083<211> 534<212> DNA<213> Homo sapien

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120aagccaactg acaaagatgc atcacgtgtc ttaggctgat gccactaccc gatttgttta
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199

<210> 1085<211> 469<212> DNA<213> Homo sapien

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199

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323

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414

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378

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320

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<210> 1093<211> 473<212> DNA<213> Homo sapien

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<210> 1095<211> 414<212> DNA<213> Homo sapien

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 414

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226

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312

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234

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<210> 1133<211> 327<212> DNA<213> Homo sapien

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<210> 1134<211> 378<212> DNA<213> Homo sapien

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547

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96

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117

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255

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224

<210> 1142<211> 337<212> DNA<213> Homo sapien
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337

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<210> 1144<211> 552<212> DNA<213> Homo sapien
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344

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213

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311

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326

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159

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357

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563

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135

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 392

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<210> 1167<211> 263<212> DNA<213> Homo sapien
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<210> 1170<211> 348<212> DNA<213> Homo sapien
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246

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<210> 1179<211> 196<212> DNA<213> Homo sapien

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 196

<210> 1180<211> 635<212> DNA<213> Homo sapien

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<210> 1181<211> 460<212> DNA<213> Homo sapien

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694

<210> 1183<211> 556<212> DNA<213> Homo sapien
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556

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363

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290

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234

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703

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279

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<210> 1205<211> 103<212> DNA<213> Homo sapien
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<210> 1207<211> 431<212> DNA<213> Homo sapien

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618

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<210> 1231<211> 326<212> DNA<213> Homo sapien

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180ttcagcccta accgctactg gctgtgtgct gccacaggcc ccancatcaa natctgggat
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326

<210> 1232<211> 256<212> DNA<213> Homo sapien

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120tgaaggtgtt tacgcccag atgaaacaga attctatttg ggcaagagat gcgcttatgt
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240ctggggaaaa gtaact
256

<210> 1233<211> 312<212> DNA<213> Homo sapien

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120cagctccaga gtcaccaggt gggcgccgca gctccgctg gccgaggtct tgttgggggt
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312

<210> 1234<211> 331<212> DNA<213> Homo sapien

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331

<210> 1235<211> 380<212> DNA<213> Homo sapien

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240cacaacatng gtcgcaaant tgtgctgact caatacaant acattgcctn gganctgct
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380

<210> 1236<211> 372<212> DNA<213> Homo sapien

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372

<210> 1237<211> 102<212> DNA<213> Homo sapien

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102

<210> 1238<211> 467<212> DNA<213> Homo sapien

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120ccgtcagctc taaagggtac tgancgttaa tggagggcgg gagcangaag aaaagtccang
180acctggcaaa agatcatct tccctccata tcctttctga ggtaatatata ngtaaaactga
240nacctggacc agagggtcga attatatcca tagtcacctt tattctgaat taaccattta
300tcaagagtgc gcctgaaaag agtagaaaaa aataaaggag cccatcaaaa aaaagttccc

360tggcaaagtg ggaggaggga catnatgtta ggagccctgt ttggggaagg aaatgttttc
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467

<210> 1239<211> 264<212> DNA<213> Homo sapien
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120atgcagcttt tgcaaaagcg ggggcccgtt tccctcctag cccttcagct tgctcaccct
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264

<210> 1240<211> 176<212> DNA<213> Homo sapien
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120aaacagaaaa attcatgagc caaaaaaaaa anccaaaaaa aaaaaccg cgaaaa
176

<210> 1241<211> 301<212> DNA<213> Homo sapien
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300g
301

<210> 1242<211> 108<212> DNA<213> Homo sapien
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108

<210> 1243<211> 142<212> DNA<213> Homo sapien
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60acaacacat agccagtata tttagtttg cttttcctaa catagaaatc ttcaaagctg
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142

<210> 1244<211> 559<212> DNA<213> Homo sapien
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120acattgggga cacattgagc agggcttgaa agaatcagga ttctgaacc ttggatcaca
180cctccagatt tgcaagagaa aatccacatt ttgcccacaa aatgtctatt cttgacggag
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559

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277

<210> 1246<211> 256<212> DNA<213> Homo sapien
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256

<210> 1247<211> 550<212> DNA<213> Homo sapien

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550

<210> 1248<211> 108<212> DNA<213> Homo sapien

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108

<210> 1249<211> 240<212> DNA<213> Homo sapien

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240

<210> 1250<211> 553<212> DNA<213> Homo sapien

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420aaatgtggcc ctgtccgggg tactgactcc gtccccctta gagttcccca ccaaggactt
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553

<210> 1251<211> 246<212> DNA<213> Homo sapien

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246

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420agncattgtg ctctgggttn tccacttcca caacaccca nggtagagg cggnccttga
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550

<210> 1253<211> 245<212> DNA<213> Homo sapien

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120ggggatgcaa acgtgcaaaa gcagggggaa gctgccagg ctgagactgg agcagctagg
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245

<210> 1254<211> 556<212> DNA<213> Homo sapien

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556

<210> 1255<211> 494<212> DNA<213> Homo sapien

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494

<210> 1256<211> 312<212> DNA<213> Homo sapien

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312

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441

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339

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376

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65

<210> 1262<211> 177<212> DNA<213> Homo sapien
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177

<210> 1263<211> 560<212> DNA<213> Homo sapien
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556

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549

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246

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143

<210> 1268<211> 447<212> DNA<213> Homo sapien
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262

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289

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90

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381

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183

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261

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383

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512

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384

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112

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287

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313

<210> 1337<211> 431<212> DNA<213> Homo sapien
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431

<210> 1338<211> 535<212> DNA<213> Homo sapien
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240ttactaaagg gagggaaga ggccaggtgg gccgctgact gggccatggg gagaacgtgt
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420ctgttgnggg gattaaanng ctcggtgan tgaaggacac atcaccttcn tgttcanag
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535

<210> 1339<211> 317<212> DNA<213> Homo sapien
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317

<210> 1340<211> 543<212> DNA<213> Homo sapien
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360acaaatgtat ttgcaaatgt tcacaaatgc taacaggagg ctggtggtt gatgcatgtg
420gnccttccaa cttgaacgga atgtactatc cacagaggca gaacacaaat aagttcaacc
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543

<210> 1341<211> 536<212> DNA<213> Homo sapien
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120aagtgcggca gcaccagggc agcccaaagc agggctgctg tgaaaatata aaagtatctc
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240cagtcagcat ctattcttgg gcaccgggag gagccgctct ctggaatctt aaattaccag
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536

<210> 1342<211> 539<212> DNA<213> Homo sapien

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539

<210> 1343<211> 224<212> DNA<213> Homo sapien

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120ctgcgttggc ggtgcagtat tcttcattat tgaacatata gctggagtgg tcttcagaat
180cctgccttct gggagcactt gggacagagg aatccgctgc attc
224

<210> 1344<211> 408<212> DNA<213> Homo sapien

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120aggggtgcgat gatgacctac agtcaatgac ttagacaagg gcgatgccag tggggcttgg
180tatgtttctc agcatcatta cccatgccat ccccatcag aggttgtgga gcagctcgtg
240cgacctctcc ttcaaatggg ctttagggaa agttaaatgg gagtgaacca gacaatggtc
300actcaaaaga ctacataaa tgagtctcct gctcttcac aagcaattaa gaccagttcc
360ccttctagt gaaataagac gtcaaatata aagttttaag agaagcaa
408

<210> 1345<211> 177<212> DNA<213> Homo sapien

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120gctctgtatg ggaggccatg gccttcgcca gcactataa gctggacaac cttgtgg
177

<210> 1346<211> 219<212> DNA<213> Homo sapien

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120ttaagcaagc aatgtcattt ttgaaactaa caggtttgtg tgtttttttt tactcaactt
180cttttttttt ttataaaagg tacacttctg tttatattt
219

<210> 1347<211> 538<212> DNA<213> Homo sapien

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180tggcagcatc aggatcacac ttgaaggggc tctcagacaa agttgtattc atgctattaa
240ataaaacaaa agtagtcata agacaaaata acaaaaatta tctcttaaga gttaaaaaat
300gagttgaaag tggttgacca ggtgatattc aagtttagtt tagtcgaaag ctttttcacc
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420attcaaatat cttacaagt tcggatttaa gaaactgaga ttgggctagg tgtgtggct
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538

<210> 1348<211> 290<212> DNA<213> Homo sapien

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120gaaaacacat aaacacctgg gtatctgaaa agacagaagg taaaattgcg gagttgctct
180ctccgggctc agtggatcca ttgacaaggc tggttctggt gaatgctgtc tatttcagag

240gaaactggga tgaacagttt gacaaggaga acaccgagga gagactgttt
290

<210> 1349<211> 540<212> DNA<213> Homo sapien

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540

<210> 1350<211> 243<212> DNA<213> Homo sapien

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120cacttggcac acagggttgt atgtatgtgt atatatatgt gtatgtatgt atgggtgtgg
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240ctt
243

<210> 1351<211> 382<212> DNA<213> Homo sapien

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382

<210> 1352<211> 535<212> DNA<213> Homo sapien

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535

<210> 1353<211> 412<212> DNA<213> Homo sapien

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240agtccagaaat ctgttctatt ctgctccagg aaaatcgga acctgtgagt cagagtcaga
300gaaacttacc caagcaacgt aattcctgtt tcatgggtc ctgtagatgt ttgagttcan
360gaangtaagg cggggagtga ctgaataaaa ctcttgctt ttacctcggc cg
412

<210> 1354<211> 85<212> DNA<213> Homo sapien

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85

<210> 1355<211> 427<212> DNA<213> Homo sapien

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60gncngngccn angtcagaga tggctnntnc atttgnccac tgagaaatta gaaactaggg

120gcaaggggga ggaaaagtac tgaaatacag tttatgaagc aagtgtgtct cgggctgtgc
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427

<210> 1356<211> 266<212> DNA<213> Homo sapien
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180tggtgattag tcggttggtg atgagatatt tggaggtggg gatcaataga gggggaata
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266

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240ctgtggggtt tttcttgtaa nactgagga tgacttntat gattggcgcc ancaagtcaa
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343

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102

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486

<210> 1360<211> 181<212> DNA<213> Homo sapien
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120ccaggaactg ctcgccagga tccccagagc gaatggctcc catgcttcgg acaccacag
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181

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269

<210> 1362<211> 124<212> DNA<213> Homo sapien
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124

<210> 1363<211> 276<212> DNA<213> Homo sapien

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276

<210> 1364<211> 270<212> DNA<213> Homo sapien

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270

<210> 1365<211> 180<212> DNA<213> Homo sapien

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60gtcactaata gaatgtctcc aaagctggat tgatgtggag aaaacacctt tcccttctag
120ttttgagaga cttcctcttg gctcccagga ggagggattc cctgactttg acacacatgg
180

<210> 1366<211> 211<212> DNA<213> Homo sapien

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211

<210> 1367<211> 179<212> DNA<213> Homo sapien

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120ccactatgat gggaaacatt tcattcccaa aaaaaaaaaa aaaaaaaaaat ncntttttt
179

<210> 1368<211> 384<212> DNA<213> Homo sapien

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300aatagtccag cccattgagc tcctgtgcga tggcggcaat ctgctccaca cggctctggt
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384

<210> 1369<211> 241<212> DNA<213> Homo sapien

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120ttccctgcaa agtagcgcca aaactggggt ctcttgtcca caccaccag gaagatctgc
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241

<210> 1370<211> 302<212> DNA<213> Homo sapien

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302

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277

<210> 1372<211> 462<212> DNA<213> Homo sapien

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360ctgggtcaagg acctcggcnc gngaccacgc taaagggcga aattccanca caacttggcg
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462

<210> 1373<211> 241<212> DNA<213> Homo sapien

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241

<210> 1374<211> 133<212> DNA<213> Homo sapien

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133

<210> 1375<211> 495<212> DNA<213> Homo sapien

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180ggataactag gaaattattg taagtaatgt tttatttcag tacttagcaa ttagagttct
240tttattaaga tgtatctgct ggattaaggg tacagggtga aatagtctg tggctgccta
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360ttttctgttt acatatactt tttttaatag caatggggnt tttattaaaa catgctgngg
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480accctaangg cgaat
495

<210> 1376<211> 110<212> DNA<213> Homo sapien

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110

<210> 1377<211> 171<212> DNA<213> Homo sapien

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120catgattgac gacgtcgcg atggaggta ccaacttgat gatcagcttg g
171

<210> 1378<211> 494<212> DNA<213> Homo sapien

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180atttttttac tggctgcccc aaggccaaga catgcacctt cattctccgt ggccggcgccg
240agcagtttat ggaggagaca gagcgggtccc tgcattgatc catcacgac gtcaggaggg
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360acctgcggga ttactcaagg actattccag gaaaacagca actgttgatt ggggcatatg
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 494

<210> 1379<211> 406<212> DNA<213> Homo sapien
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 120ctgctgtcag cttatttttc tggacttgt attttcacat gttaaattgat ctttatatat
 180gttgaattaa caaatatttt gagtttctga gaaaaaaca aacatattaa tggatttgaa
 240atgtgttagt agtctggctg tgtgccaaa attctgttgc gcagcaaaag tgaagacctg
 300tatgtaaaga aagtataaca attatttctt tgtatttttag gggctttaac cggaacatcn
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 406

<210> 1380<211> 509<212> DNA<213> Homo sapien
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 120gcatatgaag aagttctgaa ttatcaatct ccaacaacat gccagtgtt ttaccagcaa
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 360ccaactctg caccatattt atactgntgg aacgggtcgg acagcaggag taacttgac
 420cggctncaag ctncaggacg tgggacccat ttgntctgtg ttgatgtggn naanaacacc
 480cttgngtnga ctacttctnt gggaaccnn
 509

<210> 1381<211> 256<212> DNA<213> Homo sapien
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 120cagttaggag gatgccaagg ctgccaanga ggcatggaa gacgggtgaaa ttgatggaaa
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 256

<210> 1382<211> 441<212> DNA<213> Homo sapien
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 120ccatgtgtgt cctcaaggac agggaactgg ggaactggcct caaagtaggc attagaataa
 180actgccaca ncagtttaat gtggagaggt gtaaaatatt tgaaccttcc ttataaacac
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 300nctttnatcct tgntaaccac ggaagctnt tacttgctt ggccttcaaa gaaacttggg
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<210> 1383<211> 296<212> DNA<213> Homo sapien
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 120cattccgatt cctgtccctt ttgggtact ttggggagac tctggctccc aggatctgtt
 180ccctatttca gtgccttctt angacacagg ggactccttn acgctoccca ggccttctnt
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 296

<210> 1384<211> 406<212> DNA<213> Homo sapien
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 60aacagaagac gagaactttt gctgtaagtt caaaagttac ttctatgtct acacaaacaa
 120aagtgcagaa ttcccaaatg aagatggctg gagcaatgtc taccacagca aaaacaatgc
 180aggcagttaa caagaagata gatccacaaa agacattaca acaatgcag aatttccaga
 240agggaaacat gaaaatggaa atgactgaag aaatgatcaa tgatacactt gatgacatct
 300ttgacgggtc tgatgacgaa gaagaaagcc aggatattgt gaatcaagtt cttgatgaaa
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406

<210> 1385<211> 504<212> DNA<213> Homo sapien

ccaactatgc ctctcagaac atcacctacc actgcaagaa cagcattgca tacatggatg
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120ttgctgaggg caacagcagg ttcaattaca ctgttcttgt agatggctgc tctaaaaaga
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504

<210> 1386<211> 488<212> DNA<213> Homo sapien

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120gggtgtgggc cgaagatatg ctcatgtggt gttgaggaaa gcagacattg acctaccaa
180gagggcgagg gaactcactg aggatgaggt ggaacgtgtg atcaccatta tgcanaatcc
240acgccagtag aagatcccag actggttctt gaacagacag aaggatgtaa aggatggaaa
300atacagccag gtcctagcca atggtctgga caacaagctc cgtgaagacc tgggagcgac
360tgaagaanat tcgggcccat aganggctgc gtcacttctg gggccttcgt gtccnaagcn
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480aanattgt
488

<210> 1387<211> 502<212> DNA<213> Homo sapien

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120gcaggggtgg gcacctctc catttgatag aaactttgga accaaaatct ctgccagagc
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240cgatgattcc atttgtgtgc tgggaataag caaaagaaac gttatttttc aacctgtggc
300agagctgaag aagcaaacgg attttgagac ggtttccatg cagccgccgc ggtgaactcc
360cctctggtgg acactcccc agggcctcgg tgtgatggag tttcctgaat cagcgangga
420nacgtgggga cacccttng cacccttctt tttacttctg tttttacctc ggccngcccc
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502

<210> 1388<211> 508<212> DNA<213> Homo sapien

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60gcactcatta ggaaaatgca agtccaaacc acaatgagat gccacctgaa accaatcagg
120atggctgtta tcacacacct acacacacac atacacacac acagagcaag gttggcaag
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240atacccaaag gaaataaata tatacccaaa ggaaatgaaa tatttgcaa tatncaaaag
300gtagaagtaa cccaagtgtc cattgtctga ggggatggat aaccaagat gtggnacata
360catattaatg aagtattatc cnccttaaaa ggaatggaat ttttgacccc tacttccact
420tgggatgaac cnccaaaaan attattatta ttattgntt tattttttt ttttttgaa
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508

<210> 1389<211> 539<212> DNA<213> Homo sapien

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60ctctggagta aaatatgctg catccgggca agaattctta agactgaacc acaaagaggt
120aaggctctnc aaagagatgg accgacctt gggttaggca gcccttctgc cccagagaaa
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360ccantnttga tncctggga agaattacca cttcccttgc ttaannaccc aagcgaagga
420gtctttttng naagggggcg ggnattggg nccntatttt ncccccntg gntttttcc
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539

<210> 1390<211> 326<212> DNA<213> Homo sapien

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120tgaggctcag aacacaacct acctgtggtg ggtaaattgt cagagcctcc cagtcaagtcc
180caggctgcag ctgtccaatg gcaacaggac cctcactcta ttcaatgtca caagaaatga
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326

<210> 1391<211> 234<212> DNA<213> Homo sapien

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120ggccttgccg tgcatccttc ccacgctggt actttgacgt ggagaggaaac tcctgcaata
180acttcatcta tggaggctgc cggggcaata agaacagcta ccgctctgag gagg
234

<210> 1392<211> 403<212> DNA<213> Homo sapien

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60actggctagt cgaccggtcc tgtaccgtcc tcaatgtaga aggtgacgct ctgggggagcag
120gactcctcca aaattacgtg gaccgtacgg agtcgagaag cacagagcct gaggttgatac
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300tcatgtaaac cccgggaggg accttccctg ccctgctggg ggtgctcttt ggacactgga
360tttatnagga atggataaat gnatgagctn aggtctcttg ggg
403

<210> 1393<211> 504<212> DNA<213> Homo sapien

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60tccttctgcc tcagcctccc aaagtgtga gattacaggc atgagtcacc atgcccagact
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360ctttcctctt cttgacagtc tgatgggaaa caaaggcaca cataagagcc tattccaagt
420agtcaacacc tgaaaggaag ggatatggag aagtaatnct tcatatctcc aggaatgcct
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504

<210> 1394<211> 267<212> DNA<213> Homo sapien

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120ctaagaaagt ggcctggaga tgtttagaag gttaaaacca acgaagaaga aatcaatga
180caacctatca ggaactgatt gactctcaga atggagaact ggacacagaa actggatcat
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267

<210> 1395<211> 378<212> DNA<213> Homo sapien

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300ggatgataac acgctatgat ctgtaccaca ccttcgggcc agctgtcctc ctgctgatgt
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378

<210> 1396<211> 259<212> DNA<213> Homo sapien

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120tcaaaagcca actctgagga gagcaagtgg cagaacagc ccttgggctc cctccccag
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240gcgcgccgga taaggttgg

259

<210> 1397<211> 508<212> DNA<213> Homo sapien
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508

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409

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199

<210> 1400<211> 439<212> DNA<213> Homo sapien
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439

<210> 1401<211> 570<212> DNA<213> Homo sapien
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60ccaagcccag aagtgttacc gggacttagc tctggtgagt cgtgatggca tgaatattgt
120cctgaataaa atcaaccaga tacttatgga gaagtacctg aagctgcagg atacctgccg
180tactcagttg gtgtggttg tacgggaact ggtgaagagt ggggttctgg gagccgatgg
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420tgcccagntt caggncctgc gacaagaagg aagtanactt ctgnatctca ctgnttnggg
480aacggttcat ggaatntctt gatnaatggg tcgggatctc gtaaaaaannt actttcanaa
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570

<210> 1402<211> 294<212> DNA<213> Homo sapien
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60aattcagagg caacacctgt gcatctgtcc caccaaagggt gctttaatac ctaccttcac
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240gccaagctct gactaacttc tggtatgaa aataaggaaac ttgccagca tagg
294

<210> 1403<211> 635<212> DNA<213> Homo sapien

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120agggtgcagaa actgcagatg gaagctcccc acatcatcgt ggggtaccct ggccgtgtgt
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635

<210> 1404<211> 566<212> DNA<213> Homo sapien

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120ccttctgacg accaagaaaa aatggaaaga ctgtaagatc agagtattca ttggtggaaa
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420tttataagac caagacatac ccggcagatc aggttaaag agttattaaa ggaacattca
480agcacagcct aatattattg tcattgngt ctcccaattg caccaaaaag gngctgngt
540nagtgncttc ttacatggca tgggtt
566

<210> 1405<211> 103<212> DNA<213> Homo sapien

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60ctacttcctc agtgatgtgg accaggggggt gggtagactg ggc

103

<210> 1406<211> 384<212> DNA<213> Homo sapien

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120tctgtgacca gtgggacaat ctgggggcc taactcagaa gcaaggga gctctggagc
180ggaccgagaa actgctggag accattgacc agctgtactt ggagtatgcc aagcgggctg
240cacccttcaa caactggatg gagggggcca tggaggacct gcaggacacc ttattgtgc
300acaccattga ggagatccag ggactgacca cagcccatga gcagttcaag gccaccctcc
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384

<210> 1407<211> 226<212> DNA<213> Homo sapien

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120caactgttgc caaagagttg gctttgttta ttgtgtttg gcggggagag gagtggtatt
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226

<210> 1408<211> 413<212> DNA<213> Homo sapien

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413

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441

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453

<210> 1411<211> 565<212> DNA<213> Homo sapien
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297

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120acacattcac acagctgttc cctcgcattg tttttcatga acatgacctg ttttcgtgca
180ctagacacac agagtggaa agccgtatgc ttaaagtaca tgggacagtg ggactgggaag
240tgacctgtac aagtgatgca gaaaggaggg tttcaaagaa aaaggatttt gttt
294

<210> 1414<211> 592<212> DNA<213> Homo sapien
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<210> 1415<211> 218<212> DNA<213> Homo sapien

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218

<210> 1416<211> 434<212> DNA<213> Homo sapien
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434

<210> 1417<211> 381<212> DNA<213> Homo sapien
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381

<210> 1418<211> 425<212> DNA<213> Homo sapien
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<210> 1419<211> 122<212> DNA<213> Homo sapien
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122

<210> 1420<211> 686<212> DNA<213> Homo sapien
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686

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413

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643

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284

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243

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123

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419

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691

<210> 1429<211> 125<212> DNA<213> Homo sapien

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125

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116

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241

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133

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234

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294

<210> 1435<211> 674<212> DNA<213> Homo sapien

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 674

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 365

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222

<210> 1441<211> 725<212> DNA<213> Homo sapien

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600anaaccctta caagtttcag ggttcttgg aaattttacc annggccctt ttganaggaa
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720ngggn
725

<210> 1442<211> 294<212> DNA<213> Homo sapien

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120ttgccagctc atatatataa tcacagagag tgtggagaaa taagtcatct aaaatctttt
180gcagaatctc agggaaaccgt aaaatgcacc ggcctagttt ccattccttc tcatgatcca
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294

<210> 1443<211> 390<212> DNA<213> Homo sapien

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120cctccatcca gttgttgaag ggtgcagccc gcttggcata ctccaagtac agctgggtcaa
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390

<210> 1444<211> 156<212> DNA<213> Homo sapien

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60aataagggtg ataagtacaa tgtattctaa aactgttaag caaaaaaaaa aancaaaaaa
120aaantccagg ngncctcctc cncnctcnc cctggg
156

<210> 1445<211> 706<212> DNA<213> Homo sapien

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240tccactacat tgatgagcta ctcatcccag actcagccaa gacactatct gaattggctg
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706

<210> 1446<211> 503<212> DNA<213> Homo sapien

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503

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120tctctccgatt tatattaaaa attcacacac aaatgaaaat ggaaaaactg ccaatacctg
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304

<210> 1448<211> 637<212> DNA<213> Homo sapien
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120cagttaccac agcctagata cgcgttagat gcgccttttc cggcctgtgc gtctgctctg
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420gtttattttt gtaactgggt tacatgttcc gattagttaa tcngnagctt attgtcattt
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637

<210> 1449<211> 279<212> DNA<213> Homo sapien
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120ggtcattcca gaaggccag gagaaactgt gggaataaat aaaacctccc tctctccact
180ggcggcaagt gctgttttaa gcaaaatcct catttcaatg tgagggtag aaactattc
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279

<210> 1450<211> 317<212> DNA<213> Homo sapien
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120gaaagatcct catgaattaa atagttgatg caatttttaa cgtaattga tataaaaaaa
180aacaacaaaa ttaggcttgt aaaactgact ttttcattac gtgggttttg aaatctance
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317

<210> 1451<211> 297<212> DNA<213> Homo sapien
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180ggcgagggtc acatttcacc atctggttgg ctggctcaaa gcaagcattg gtgatctctg
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297

<210> 1452<211> 445<212> DNA<213> Homo sapien
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60tggaatagtg gtagtgagg gatgagcaat ggctgggggt ggtgttaagg aaggtgatac
120aaattctttt tctataacag ttccagaaaa agcctcaggt gttactgata agggcaaaag
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445

<210> 1453<211> 302<212> DNA<213> Homo sapien
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302

<210> 1454<211> 372<212> DNA<213> Homo sapien
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180aaaaatcttt aatttggttg agtaaaaacc aaattagttc actgaatctc attttgtagg
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300cacaggataa ccagtattag tggagaacac tacaaaagggt ggcttggtgt gatttctttg
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372

<210> 1455<211> 310<212> DNA<213> Homo sapien
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120cttcttcagt cgctccaggt ctccacggag ctgtgttcc agaccatttg ctaggacctg
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310

<210> 1456<211> 344<212> DNA<213> Homo sapien
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240tgccagactg gagtgcatg gtgcgatctg ggctcactgc aatctccacc tcccgggttc
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344

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332

<210> 1458<211> 540<212> DNA<213> Homo sapien
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420accagggtgt taatctttat gtgaaaaate ttgatgatg tattgatgat gaacgtctcc
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540

<210> 1459<211> 223<212> DNA<213> Homo sapien
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223

<210> 1460<211> 368<212> DNA<213> Homo sapien
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368

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290

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535

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484

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267

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231

<210> 1466<211> 202<212> DNA<213> Homo sapien
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120tggaactgtg tttttttctg ctttgtttt tcagtttgct gtttctgtag ccatattgta
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202

<210> 1467<211> 97<212> DNA<213> Homo sapien
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97

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342

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308

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284

<210> 1471<211> 490<212> DNA<213> Homo sapien
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286

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230

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330

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120agacactcaa gtccaacaac tcgatggcac aagccatgaa ggtgtcacc aaggccatgg
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197

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180gacaaagaca cagtgtgtgt ggagttttat gctccatggg gtggacattg caagcagttt
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360ctggagtgtc cacagtctcc tgggagagga gcaccacccc agacattact ggttatagaa
420ttaccacaac ccctacaaac ggccagcagg gaaattcttt ggaagaagtg gtccatgctg
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538

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120gntagaagtg aggtgtgag caggagcctc tgccagggga tgcacatct gtggggaggg
180gccgaggag actccatggg ctctgtgtc tgcctgtgag tgcctgtgag agaagagctt
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288

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141

<210> 1480<211> 388<212> DNA<213> Homo sapien
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120cagagggttg agtgagccga gatcagcca ctgactcca gcctgggcca cagagcgaga
180ctccatttca aaaaaaagaa ctacaagttc tgattccgga ctccagatg tgagttttaa
240tctcctctcc actgattgat cctgactaat cactagcccc ctgtgcccaa tttcaacagt

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388

<210> 1481<211> 541<212> DNA<213> Homo sapien
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240ggggcctcct ttcacctag ttcattgaagc cccaacactt cctccctggg atcagtacca
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540g
541

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424

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431

<210> 1484<211> 99<212> DNA<213> Homo sapien
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99

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120tgtctctatg tggctcccgg aattgctgag gtctcacttc tcagagggtc ttgatggaaa
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192

<210> 1486<211> 98<212> DNA<213> Homo sapien
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98

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120ggagttgttt tcagctataa cacggattcc cgccagacgt gtgctaaca cagacaccag
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240cggccgctcg aaggg
255

<210> 1488<211> 261<212> DNA<213> Homo sapien
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120gctgaacttt caagtgatgt catcttacta ctgagaagtg agagagagggt ctttaaggggt
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261

<210> 1489<211> 344<212> DNA<213> Homo sapien
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180ttcaagagta caggtcagag tcttcttttc ttttcttttt gagatggagt cttgctctgt
240tgccagactg gagtgcagtg gtgcgatctg ggctcactgc aatctccacc tcccgggttc
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344

<210> 1490<211> 426<212> DNA<213> Homo sapien
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300cagcgtcatc agagtcgcag gcattggcgtc ctcttcacc actgcgctgc ggaaccacac
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426

<210> 1491<211> 339<212> DNA<213> Homo sapien
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339

<210> 1492<211> 543<212> DNA<213> Homo sapien
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543

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77

<210> 1494<211> 344<212> DNA<213> Homo sapien
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180gtgaacctca gcctctcctg ccattgcagc tctaaccac ctgcacagta ttcttggtg
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344

<210> 1495<211> 380<212> DNA<213> Homo sapien

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380

<210> 1496<211> 540<212> DNA<213> Homo sapien

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540

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120tgcttggata gtcagtcaat tatttgtgta tgaaacaatg tacaatatcaa tgttttgaaa
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212

<210> 1498<211> 204<212> DNA<213> Homo sapien

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120caagagcggg ctctctcctg agataagaca agtttaacgt gaagaccttt tggaaaattc
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204

<210> 1499<211> 305<212> DNA<213> Homo sapien

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305

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547

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<210> 1502<211> 278<212> DNA<213> Homo sapien
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278

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591

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330

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120antttttttt naatnnggn aaaanttttt tncccnaaa aaaaaaattt tt
172

<210> 1506<211> 144<212> DNA<213> Homo sapien
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60agagacaggg gaggaggaa gaaggatact gtggaaaggg atggcggggc aacatttan
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144

<210> 1507<211> 303<212> DNA<213> Homo sapien
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303

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52

<210> 1509<211> 80<212> DNA<213> Homo sapien
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80

<210> 1510<211> 415<212> DNA<213> Homo sapien
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 126

<210> 1512<211> 331<212> DNA<213> Homo sapien

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<210> 1514<211> 170<212> DNA<213> Homo sapien

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<210> 1515<211> 174<212> DNA<213> Homo sapien

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 120gtgagtcgta ttacaattca ctggccgctg ttttacaacg tcgtgaatga gaan
 174

<210> 1516<211> 481<212> DNA<213> Homo sapien

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 120ccagggcctc ccggaagtca aggagaaagt ggtcgaccag gtcctcctgg gccatctggt
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42

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571

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117

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123

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336

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438

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308

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87

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344

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122

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373

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373

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221

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555

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358

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410

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335

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238

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276

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344

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